BLOOD TRANSFUSION

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BLOOD TRANSFUSION

BY

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PREFACE

Two thirds of this book is an account of my own personal experiences with blood transfusion The remainder represents an attempt to extract the more important material from the vast literature that has collected around the subject

My purpose has been to present the practice of blood transfusion

All subjects not directly related to blood transfusion have been omitted—for example the medico legal and anthropological aspects of blood grouping—and, to economize space, there is no historical section

In matters of technique, where several alternative methods or patterns of apparatus exist, as for example in the technique of blood grouping or in the choice of transfusion apparatus, I have adopted the principle of describing in detail the procedure which I have found by experience to be the most practical, to the exclusion of the rest This is in contrast to the continental custom of describing a variety of methods, as the result of which the reader is no doubt better informed but is left in some confusion as to which to employ in practice

I have drawn particular attention to the grave danger of circulatory failure in the transfusion of anaemias of long standing, and to the principles governing the rate of introduction and dosage of blood, as altered conceptions in regard to these matters form the two most important advances in blood transfusion of recent years

A technique for estimating the titre of typing sera is included, as the provision of typing sera of guaranteed potency is a matter of fundamental importance

A simple diagrammatic plan for explaining the interaction of the blood groups is illustrated

A new composite transfusion apparatus—the transfusion unit—is described

The organization of a voluntary transfusion service is discussed at some length

The international nomenclature is applied to the blood groups throughout

The chapter on stored blood is incomplete, but it was

necessary for me to stop adding to this section if the book was ever to be published, and I have tried to compromise by making the bibliography as up to date as possible

It is now nearly twenty years since the subject of Blood Transfusion was reviewed in book form in this country, and during this time an immense bibliography has collected No attempt has been made to represent this fully and only those contributions which seemed to me to be of practical importance have been extracted for quotation The Harvard reference system has been adopted

VICTOR RIDDELL

26 HARLEY STREET W 1
September 1939

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My thanks are due to the Association of Surgeons of Great Britain who by electing me their Moynihan Fellow enabled me to visit and see blood transfusion in most of the countries of Europe and many of the large cities of Canada and the United States of America, to the Staff of St George's Hospital, where as Surgical Chief Assistant I was able to develop my interest in blood transfusion, and to the Staff of the Royal Waterloo Hospital where I have had experience with younger patients

In particular I have also to thank

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I have frequently referred to GEOFFREY KEYNES s *Blood Transfusion* which has withstood the test of time for nearly twenty years WHITBY AND BRITTON s *Disorders of the Blood* WIENER s *Blood Transfusion and blood groups* SCHNEIDER s *Blood groups* and LATTES *Individuality of the Blood* and I wish to record my indebtedness to these authors

My special thanks are respectfully tendered to P M R for associating with me during this enterprise and to A S R for numerous constructive criticisms

While I was abroad I was fortunate in being able to discuss transfusion with some of the leading authorities in Canada the United States and on the Continent and I would like to express my gratitude in particular to

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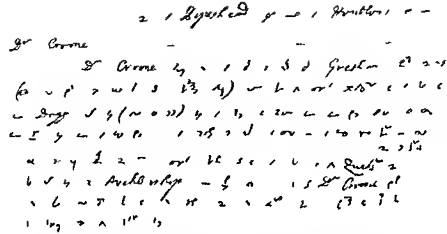
V H R



myself to the Pope's Head. Here Dr Croone told me that at the meeting at Gresham College to-night, which it seems they now have every Wednesday again, there was a pretty experiment of the blood of one dogg let out, till he died, into the body of another on one side, while all his own run out on the other side. The first died upon the place, and the other very well, and likely to do well. This did give occasion to many pretty wishes, as of the blood of a Quaker to be let into an Archbishop, and such like; but, as Dr Croone says, may, if it takes, be of mighty use to man's health, for the amending of bad blood by borrowing from a better body.

DIARY OF SAMUEL PEPYS, November 14th, 1666

Reproduced by courtesy of the Pepys Library, Magdalene College, Cambridge, and the Wellcome Historical Medical Museum

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'It is sufficiently knowne that mans body is joined together of four kinds of humors or complexions to wit, of BLOUD, Cholera, Melancholia, and Phlegma, *but amongst these is the bloud one of the best, partly,* for that it is the matter of the vitall spirits, wherein life itself hath his being or for that it is to be compared with the beginning of life, because it is by nature warm and moist or because it hath more vertue to nourish and to sustaine, than any of the other humors

In fine, it is such a Jewell of nature, that if the same be taken away, then death doth ensue'

Wirtzung's *General Practise of Physicke*
London 1617

CHAPTER I

THE COLLECTION OF BLOOD FROM THE DONOR

General Management

As soon as the donor has arrived for a transfusion he is asked to sit down and the cross grouping is begun straight away While this is proceeding it is as well to ask certain questions

'What group are you? This may sometimes expose a mistake clerical or telephonic at the outset and so avoid a catastrophe Occasionally more than one donor is attending the hospital at the same time and it has happened that they have been mixed

How many transfusions have you given? A donor attending his first transfusion must be at least slightly apprehensive Sympathetic and skilful handling will do more than relieve his anxiety *It is likely by giving him a good start to keep him as a* member even though afterwards he may have less fortunate experiences In the case of an experienced donor it will be worth while to ask his advice on the choice of a suitable vein *he probably knows for instance that the most prominent vein* is not necessarily the easiest to puncture

Have you just had a meal? The fasting donor is preferred

'Which arm do you prefer? Sometimes a donor would like to be able to use a particular arm that evening or soon after the transfusion for music or games

While observing the cross matching the donor is told to take off his coat and waistcoat and lie on a couch this saves a little time in an emergency and removes him from the immediate sphere of activity

THE DONOR

Position

The donor should be supine with a small pillow under his head If the blood is taken in a sitting position he may faint

The bed table or couch should be firm and preferably about the height of an ordinary operating table so that the introduction of the needle is made by the surgeon standing while the blood is collected by an assistant sitting An assistant is not

necessary if the receiving flask can be arranged at a convenient height on a side table or stool

The *apparatus* required will be

A sphygmomanometer
A collecting bottle
Donor needle size 13 (S W G)
Donor tubing (new) Length 9 inches Internal diameter $\frac{3}{16}$ inch
Sodium citrate 3 per cent For dosage see p 182
And the usual requirements for skin preparation and local anaesthesia

The upper limb

Position The arm should be to the side in the *anatomical position* and not abducted with a small firm *pillow* behind the elbow to throw this region well forward Most donors like to have something in their hand to grip such as a bandage

Venous obstruction An ordinary *sphygmomanometer* blood pressure bag is wrapped round the arm above the elbow and blown up so as to obstruct the venous return without obstructing the arterial inflow Generally speaking it will be safe to go up to a pressure of 70 mm Hg but the point at which the maximum distension of the veins is produced will decide the optimum pressure for the donor concerned By means of such an armlet an even and constant distribution of pressure around the arm is obtained so that a maximum venous obstruction is produced Moreover slight alterations in pressure are readily obtained by this apparatus which can be controlled by the donor or the surgeon

A sphygmomanometer should always be used in preference to any form of tourniquet such as a length of rubber tubing applied over lint this is uncomfortable because it often pinches the skin and donors dislike it

Selection of a vein

A medium sized vein is selected in the elbow region usually the median cubital or median basilic If the veins are very prominent it is as well to avoid the most obvious one, as a very large and superficial vein is not always easy to enter In practice *the easiest vein to puncture is the palpable* rather than the visible vein The reason is that the former is well anchored by

the tissues and is less prone to slip laterally when the point of the needle comes up against it

Skin preparation.

Acetone is perhaps best for the skin because it does not smell as much as any other suitable antiseptic such as ether, and it has the advantage of evaporating quickly, as opposed to spirit which dries slowly and leaves a slippery surface, which makes the introduction of the needle difficult *Iodine must never be used* Apart from its inefficacy as an antiseptic, it stains the clothing and sometimes causes burns the latter being in fact the commonest claim for compensation made by the donors of the London Blood Transfusion Service

Local anaesthetic.

A donor should always be asked if he wants an anaesthetic, and it should be pointed out that it is a *local* anaesthetic other-

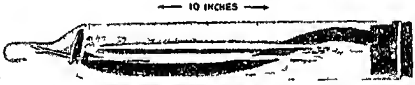

FIG 1 Donor needle and tubing in a sterile glass tube

wise some inexperienced donors imagine one is offering a general anaesthetic and refuse it promptly Quite a number however definitely prefer to have no form of local anaesthetic Considered from the surgeon's point of view the anaesthetic gives extra confidence especially with a nervous donor or if the veins are not well marked The injection should be strictly *intradermal* raising a wheal the size of a small pea care being taken not to puncture the underlying vein if this is very superficial The injection is made *over* the vein that is in the line of the vein and not to one side of it as is sometimes suggested *As soon as the anaesthetic has been introduced the blood* pressure bag should be let down, as it becomes uncomfortable if left blown up for too long, and the wheal is *massaged away* before picking up the donor needle If this is not done the wheal may obscure the line of the vein and thus increase the difficulty of the venipuncture

Cutting down.

It should be an axiom and is in fact a rule of the London Blood Transfusion Service that **the vein of a donor must never be cut down upon.** Such an injury to the donor incapacitates him personally for the time being and permanently lowers his value as a member of the Service

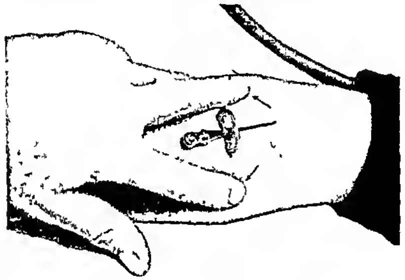

FIG 2 Venipuncture The correct technique—with *bilateral* digital control

Technique of puncture

The skin Using a sharp needle of the comparatively small bored shield mounted type, size 13 (fig 2), no initial nicking of the skin by a scalpel is necessary or advised

Control of the vein In making an intravenous injection the natural tendency is to control the movements of the vein inadequately It is not enough simply to pull the skin downwards, the vein should be controlled on either side as well To do this, two fingers must be used, *one on either side of the vein*, to stretch the skin laterally and at the same time draw it downwards (Fig 2) This position may be taken up with the hand behind the elbow or in front The former position is the easiest for children whose arms are small, the latter for adults

This method was evolved, though no doubt it is practised by many others, as the result of two years' experience in an injection clinic, and is recorded as it has proved effective

The site of puncture.

The donor needle should be introduced towards the heart at

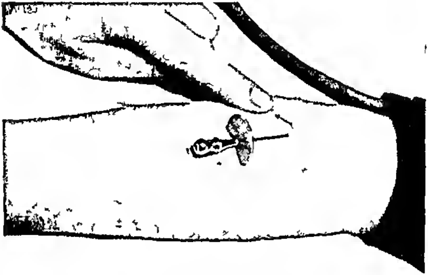

FIG 3 Venipuncture The incorrect way with unilateral control only

the *most* distal *point* in a long stretch of vein This allows for another attempt into the same vein at a higher level should a haematoma form as a result of unsuccessful initial puncture

If venipuncture is unsuccessful and there is any leakage immediately let down the pressure bag and massage away the swelling A haematoma will only form if pressure is maintained after wounding the vein

Failed puncture

Before attempting a second venipuncture the needle should be washed through with citrate Very often there is an obstructing clot present

Failed puncture may be due to inexperience, to the small size of the vein, or to venospasm

Small veins. On rare occasions, if the elbow veins are small, a better flow will be obtained by inserting the needle with the

point away from the heart that is to say directed towards the hand

Venospasm Venospasm is not common but may affect all the veins in the limb as soon as the selected vein is touched by the needle The size of the veins is also quite definitely affected by the donor's emotional state at the time If the veins are in spasm the best plan is to ask the patient to exercise his arm or to place it in a hot arm bath and try again when one will usually be successful

The method of collection of the blood

The blood may be collected by an open or closed method

The open method The open method of collection has the advantage of absolute simplicity Its safety depends upon the fact that fresh blood is a highly bactericidal medium Because blood has this property it is safe to collect by an open method provided that reasonable care is taken to avoid droplet infection from coughing or talking over the mouth of the bottle

The closed method—particularly for the inexperienced—has the disadvantage of extra apparatus and should the flow stop when using this method the necessary manipulations to restart it afford opportunities for contamination such as do not occur with the simpler technique

The procedure

(a) A short length of new rubber tubing not more than nine inches long—*it is very commonly far too long*—is attached to the donor needle

(b) *Both needle and tubing are washed through with sodium citrate* The needle should never be inserted into the vein first and the tubing attached afterwards

(c) The end of the tubing is directed into the middle of the receiving bottle Otherwise blood will be splashed over the sides which tends to cause clotting as well as making it difficult to see how much blood has been collected

Rate of flow With an ordinary donor needle size 13 blood will flow at 100 c c a minute for the first 3 minutes and 500 c c can be collected in 6 minutes this is quite fast enough for all occasions in civil practice

Mixing of the blood and citrate There is no need to stir the

blood with a glass rod as it is collected nor should it be violently agitated a little gentle rotation of the bottle to ensure adequate mixing of the citrate with the blood is all that is necessary and all that should be attempted

Arrested flow If the flow of blood stops or slows and there is no haematoma which would suggest that the needle has slipped out of the vein the needle should not be moved until the following points have been checked

1 The blood *pressure* bag may have leaked and the pressure fallen
2 The blood pressure bag may be too tight and the pressure so high that the artery is obstructed and no blood is passing into the arm
3 The *needle* bevel may be resting against the anterior wall of the vein and need the hilt tilting away from the skin so as to depress the point or the axis of the needle may not be in the line of the vein
4 The *tubing* attached to the needle may be kinked blocked with clot or too long

The flow may usually be restarted by

(a) Readjusting the pressure in the armlet of the sphygmomanometer which may be too high or too low
(b) Asking the donor to open and close his hand firmly and slowly
(c) Massaging the veins on the front of the forearm with the flat of the hand from the wrist up towards the needle this manœuvre will always increase the flow if no obstruction is present in the needle

Withdrawal of the needle To withdraw the needle the procedure is as follows First *deflate* the sphygmomanometer armlet with the left hand place a swab over the site of puncture with the other hand withdraw the needle sharply maintaining firm pressure with the swab during and after the withdrawal *Keep the forearm extended till the puncture wound is sealed* as better pressure can be maintained in this position than when it is bent at the elbow The needle should be washed through with cold water immediately it has been withdrawn While this is being done ask the donor to press firmly on the swab over the site of the venipuncture with the fingers of his free hand

Dressing the elbow If the puncture wound is small and single seal the opening with a small piece of adhesive strapping this leaves the elbow joint free

If more than one puncture has been made or if there is a tendency to leakage bandage over a clean swab in such a way as to maintain pressure and limit the movements of the elbow joint

After the transfusion The donor should remain recumbent for 10 minutes and then slowly resume the upright position The bandage should be kept on until he goes to bed, when it may be replaced with a patch of adhesive plaster which should not be removed until 24 hours after the transfusion Similarly he should be advised not to use that arm for violent exercise for that period of time These precautions may not seem necessary, but experience shows them to be advisable

The closed method The closed method of collection is the one of choice for experienced operators and in all instances when the blood is to be stored A negative pressure is made in the collecting jar either by a rubber bulb by oral suction through an intervening filter by a motor tyre pump with the valve reversed or by the rotary pump Care must be taken not to exert too strong a negative pressure as this will collapse the vein so that the flow ceases or the vein may become sucked over the end of the needle producing an unpleasant vibrating sensation The length of tubing between donor and bottle should be as *short* as possible

SUMMARY

1 The donor should be lying flat while the blood is being withdrawn
2 A sphygmomanometer should be used to obtain venous obstruction
3 The use of iodine is condemned
4 Successful intravenous puncture depends upon absolute immobilization of the selected vein This is best achieved by bilateral digital control
5 The needle should be sharp and not too large
6 A short length of fresh rubber tubing should be used for each transfusion

7 The blood should not be stirred or agitated during collection

8 Various methods of ensuring a satisfactory flow of blood are described

9 The treatment of the donor both before and after the transfusion is indicated.

CHAPTER II

THE RECIPIENT

General Management

Preliminary

Ephedrine in the form of a half grain tablet should be given half an hour before the transfusion The object of this is to provide the antidote to a possible allergic or anaphylactic reaction

Omnopon—one sixth of a grain—should be given if the patient is nervous at the same time as the ephedrine

Alkalinization of the patient has been suggested as a prophylactic against a possible haemolytic transfusion reaction

Conduct of the transfusion

The patient The *patient* should be lying in a comfortable attitude in bed with the selected arm outstretched upon a firm pillow and some means of obstructing the venous return in position above the elbow If in a general ward the bed should be screened off just before the transfusion is ready to begin

The apparatus The *apparatus* should be put together and made ready for use in a side room *away from the patient and out of his hearing* This is advisable because it sometimes happens that the start of the transfusion is held up by unforeseen technical difficulties associated with the assembling or filling of the apparatus It is better that these should be corrected out of sight of the patient Only when everything required is ready and in working order should the apparatus be wheeled on a trolley into the patient s presence The transfusion can then be started immediately without delays occurring at the bedside

The easier the transfusion goes the less impressed is the patient and the more likely he is to talk and joke after it is over This is an easy state of affairs to allow to develop, but it predisposes towards a reaction

At the end of the transfusion the patient should be induced to go to sleep with the help of drugs if necessary, and with hot water bottles in the bed in case of a possible reaction The

trolley should then be wheeled out quickly and quietly, the blinds drawn and the lights turned out

After the transfusion

Leave instructions that the first specimen of urine voided is to be collected and measured and if possible examined spectroscopically for haemoglobin as a matter of interest

Leave instructions about the treatment of a rigor should this happen (p 75)

Visit the next day and inquire if the patient has had a rigor and note the temperature and amount of urine passed and whether there is any jaundice

Arrange for a blood count and haemoglobin estimation 24 hours after the end of the transfusion

In a private house

As on the occasion of any other surgical enterprise in a private house the nurse in charge should be asked to provide space and empty tables

It is very unwise to undertake a transfusion outside hospital without a nurse in attendance at least for the night following the transfusion If there has been no complication she can go first thing next morning

CHAPTER III

TYPING SERA

THE GROUP TESTING SERA

CONSIDERABLE variations exist between different centres in regard to the care shown in selection of the donors that are to supply the typing sera in the attitude towards the need for titration of the sera so obtained in their views as to the optimum titre desirable for accurate work and in the technique of collection and sampling In some countries the serum for the whole state is manufactured at a single institute in others each hospital prepares its own The extent of distribution differs also, in some countries the typing sera are available for use only amongst recognized hospitals and selected medical men in others they may be obtained by all These various systems will now be considered and the outstanding principles emphasized

THE SELECTION OF A SERUM DONOR

Personal characters required

In the course of titrating a large number of sera it has been shown (Brewer 1937) that individuals between the ages of 18 and 45 (approximately) are more suitable than the very young or the very old in whom the agglutinin content is on the average somewhat lower than during the age period between these two The sex and stature appear to have no connexion with the agglutinin titre A bulky policeman may have a lower agglutinin concentration than a diminutive girl typist It is important that the donor should be in good health and that he should not have had anything to eat particularly any fat for at least three hours before the donation as it has been found that the presence of fat in the stored serum has a definite lowering effect on the serum agglutinin concentration

Serum characters required

High titre

The most important step is to obtain from men or women fulfilling the above conditions a donor with a high titre alpha or beta agglutinin Such an individual can only be found by

titrating the sera of a series of members of groups A and B. All new recruits to the London Blood Transfusion Service belonging to these groups have their sera titrated on joining, so that a constant supply of high titre donors is available.

The Problem of Titration

The question has been raised whether the titration, that is to say the estimation of the strength of typing sera, is really

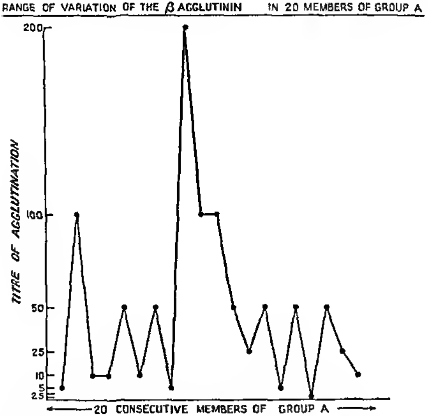

FIG. 4 A Graph to show the *variation* in Titre of the Agglutinins in members of the *same* group (Riddell and Harwood.)

necessary. The answer to this question is seen in Fig. 4 where the results obtained from the titration of the sera from 20 different members of group A are illustrated. (Similar observations have been recorded by Brewer (1937), Weiner (1935).)

It will be noticed that the concentration of the same

agglutinin varies markedly in individuals of the same group that one member of, say, group A has an agglutinin which is still active though diluted 200 times, whereas another becomes impotent when diluted only once with an equal volume of saline

This enormous individual variation shows that it is impossible to choose at random high titre sera

The Estimation of Titre Value

Collection of the serum

(a) *For estimation of Titre* About 5 c c of the fasting donor's blood should be drawn This is allowed to clot, and the clear serum is taken off as soon as it has separated, and centrifuged The serum should not be allowed to remain in contact with the clot for more than 24 hours, as there is a tendency for haemolysis to take place, which lowers the serum agglutinin concentration

(b) *For stock purposes* In putting up stock sera for supply purposes, a larger amount of blood should be drawn depending on the amount of serum required A 40 per cent yield of serum is obtainable from any given volume of blood For example, 500 c c of blood will yield about 200 c c of serum, and 1 c c of serum will fill approximately 12 capillary tubes

Technique of Titration

The principle of titration is to put up a series of increasing saline dilutions of the serum to be tested with a suspension of sensitive red blood corpuscles

Reagents required

A series of small tubes—3 in × ½ in
Graduated pipettes
Undiluted serum
Normal saline
Fresh suspension of red blood-cells of group A when titrating group B serum and of group B when titrating group A serum

Preparation of the red cell suspension.

(i) Withdraw 5 c c of blood into citrate (3 per cent)
(ii) Wash four times by centrifuging in normal saline
(iii) After the last washing, pour off the supernatant saline

(iv) Add 1 c c cells to 74 c c of 0 85 per cent saline This is now a 1 in 75 dilution

If titre estimations are frequently being determined it is an advantage to use the same cells on each occasion as the agglutinogen content varies slightly in different individuals It is convenient to take the blood from a member of the permanent staff of the laboratory

The titration

(i) Arrange 7 small tubes in a rack
The dilutions are usually chosen to be multiples of 2, but multiples of 5 are more easily remembered in the higher dilutions

(ii) Pipette the solutions in the order indicated in the diagram, fig 5, that is to say—saline first, then serum, and lastly the red corpuscles

(iii) After adding the red cells mix the contents of the tubes by inversion from high to low dilutions

(iv) Allow to stand over night at room temperature 22° C on the laboratory bench With incubation at 37° C haemolysis may occur, which makes the reading of the end point more difficult

Take readings next morning by inverting the tubes *twice* not too vigorously, and gently rolling them between the palms Shake gently and read the tubes in a good light for example directly under an electric light bulb It is necessary to take considerable time and care over determining the end point Four grades of agglutination are recognized

+++	Conglomeration of the corpuscles into a large solid mass
++	Conglomeration into a few somewhat smaller masses which may be surrounded by smaller macroscopic clumps in the fluid Or there may be one large clump and several smaller ones
+	A suspension of small but macroscopic clumps in a clear fluid (Actually in this group is included a fairly wide range of small clumps)
±	Extremely small but definite clumps detectable to the naked eye in a good light Clumps are more easily seen with the aid of a lens, preferably a ×8 If a ± is repeated, always take the first ± as the end point
—	*No detectable clumps (small amount of fibrin must not be confused with masses of corpuscles)*

It is unimportant whether the reading of tubes at the beginning of the range of dilutions is +++, ++, or + It is the *end point* which is all important

The end point will vary with the technician reading the sera, whether agglutination is determined by microscope, lens, or naked eye, with the concentration of the red cells used, and whether the tubes were incubated or not before re examination All these factors are, however, standardized by each technician and an error, if present, will be a constant one and will involve only one, or rarely two, tubes

Inhibition of haemagglutination is sometimes seen in the earlier tubes, though it may return in the higher dilutions This is the so-called *pro-zone* phenomenon These sera should not be used for typing purposes (Pondman and Brandwijk, 1932)

Test tube	1	2	3	4	5	6	7
NORMAL SALINE 0.85 per cent	0·4 c.c.	1·0 c.c.	1·0 c.c.	1·5 c.c.	1·0 c.c.	1·0 c.c.	1·0 c.c.
SERUM	1·6 c.c. Mix then add 1 c.c. of mixture to tube 2	1·0 c.c. Mix, then add 1 c.c. of mixture to tube 3	1·0 c.c.			→	Mix and discard last 1 c.c.
Dilution of serum	1 : 1·25	1 : 2·5	1 : 5	1 : 12·5	1 : 25	1 : 50	1 : 100
CORPUSCLES (1% dilution)	1·0 c.c.	1·0 c.c.	1·0 c.c.	1·0 c.c.	1·0 c.c.	1·0 c.c.	1·0 c.c.
Final dilution of serum	1 : 2·5	1 : 5	1 : 10	1 : 25	1 : 50	1 : 100	1 : 200

Theoretically and ideally an individual should be selected whose serum is free from accessory agglutinins or sub groups The only way to exclude these would be to test out the selected sera against a series of cells of the same group and of group O which are not normally agglutinated by these sera for example

A serum against A cells or O cells normally no agglutination
B ,, B ,, O ,, ,,

If these tests are negative the presence of an accessory agglutinin is extremely unlikely though absolutely to exclude one would presumably have to put up the serum against the cells of every member of those groups in the world Fortunately the presence of these accessory agglutinins is extremely rare, and even when present they are almost invariably of low titre For these reasons *accessory agglutinins may be ignored* in the selection of serum donors

The Constancy of titre of a Serum Donor.

Once a donor of high titre has been found he may be used again and again without re titration as the serum agglutinin concentration remains very constant except, perhaps for slight diminution in middle and old age The Medical Officer to the London Blood Transfusion Service (Brewer, 1937), retitrated the serum agglutinin content of 100 donors of groups A, B, and O after an interval of at least six months during which most of the individuals had donated blood on one or more occasions The repeat titration figures were identical with the originals in 91 per cent of these donors In the remainder there

was a difference of one tube only in the reading and thus can probably be regarded as an experimental error

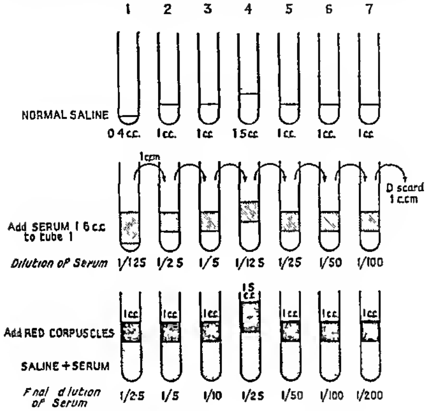

FIG 5 The technique of estimation of serum titre

I ORGANIZATION OF THE SUPPLY OF SERUM

Source of Serum central or generalized

The question arises whether ideally the serum should be prepared in a central Serum Institute as for example in Copenhagen and Utrecht, and from there supplied to the whole country, or whether it can safely be prepared in numerous smaller centres each storing enough for its own use The advantage of a central laboratory is that the serum is titrated and put up by expert serologists Furthermore, if the serum is obtainable only on application to the Institute, the destination of each tube is known and a warning notice can be sent to the purchaser a short time before the limit of potency is reached, or,

alternatively, an exchange system can be arranged for the supply of fresh sera to replace the stale Probably also, in state supported laboratories as in Holland and Denmark the centralized preparation is a better economic arrangement If the control is decentralized for instance in the hands of manufacturing chemists the system of supply and recall will be more hazardous

At the same time it would appear to be wrong in principle to deprive hospitals in particular those associated with teaching schools of the opportunity of preparing their own sera

Probably the best arrangement is a combination of the two systems the larger institutions which have the necessary staff and demand for sera to prepare their own the smaller hospitals and individual doctors to obtain commercially prepared sera provided by a reputable firm or institute on a non profit making basis

Distribution of Serum

The extent to which serum should be distributed is much the same type of problem as that of the source of supply The question has been raised whether typing serum should be obtainable by all or should only be available to hospitals and doctors of known repute Grouping is not always as simple of interpretation as it is alleged to be and it is generally agreed that blood grouping should be carried out by some one with experience whenever possible

Nevertheless if possession of typing sera is to be limited to the few the tendency will be for students not to trouble about this part of their training and eventually the number of those experienced in the use of typing serum will become fewer than ever Such specialization is not in the interests of the profession

II PREPARATION

The Relative advantages of Fluid and Dried Sera

Typing serum can be put up in capillary tubes in a fluid form or dried by exhausting in a vacuum It is claimed for the latter method that the titre of the agglutinins is maintained in the powder over a longer period of time and this is an advantage in tropical countries where the fluid forms of sera are interfered

with by evaporation For general use in most countries these claims will not apply, and as dried serum is less simple to prepare it is hardly likely to replace the fluid form except where the turnover is very small

In Leningrad, at the Blood Transfusion Institute, in an attempt to shorten the time taken in grouping, they have experimented with sera dried *in situ* on glossy paper Each plaque of serum so produced must first be dissolved with a little normal saline so that it is questionable whether in the long run time is really saved If by mistake water was used instead of saline, the cells when added would, of course, be haemolysed

Concentration of sera.

Owing to the comparatively rapid deterioration of typing sera, it may be desirable for a laboratory to supply sera in concentrated form to infrequent users, since it is the initial titre which in large measure decides the period of potency

The technique is as follows The serum is frozen solid and is then allowed to thaw undisturbed at room temperature On thawing, the agglutinins are found to be concentrated in the lower layers of the serum which are much darker than the original The top layer, which is like water, possesses little or no agglutinating power By withdrawing the upper two thirds of the thawed serum with a pipette in such a way as not to disturb the lower layers, one third of the original volume is left containing approximately two and a half times the concentration of agglutinins in the original serum The loss of total agglutinins by concentrating to this extent is therefore relatively small If greater concentration than this be required it may be achieved by pipetting off more of the supernatant and in this way a concentration as much as eight times has been obtained in the residue For practical purposes withdrawal of the upper two thirds usually suffices (O Meara 1933)

Packing.

The serum after collection must be carefully preserved from contamination as bacteria will lower the titre For most purposes the fluid form of serum is the most practicable This may be put up for use in ampoules or capillary tubes, the glass of which is conveniently coloured differently Of the two containers the ampoule which is designed to hold enough serum for a number of group determinations is the less satisfactory This is on account of the risk run of contamination

from constant reopening which is in turn followed by a lowering of the agglutinin titre

III STORAGE OF SERA

The Maintenance of Titre Value during Storage

The most important factor in assuring a prolonged period of potency will be the choice in the first place of a *high titre fasting* donor to supply the serum It has been shown that the higher the original titre the longer the serum will remain potent At room temperature and with non-exposure to light, sera with an initial agglutination titre of **1/100** will remain potent for at least six months, whilst weak sera for example 1/25 or less will deteriorate and lose all potency in a few weeks

In several of the countries visited in the course of this investigation it was found that sera of much lower titre than this were being used for routine grouping and in some titration was omitted altogether The highest titre serum was found in Copenhagen the claim being made that it was active in a dilution of 1 in 2,048 A sample was brought back to this country and on re titration was found still to have the high titre of 1 in 512 in spite of being kept under unfavourable conditions while travelling

The potency of the serum is slightly prolonged if it is stored in an *ice chest* or refrigerator and kept *away from the light*

The effect of Preservatives

The use of colouring agents added to the serum itself or the addition of preservatives such as phenol or acriflavine are better avoided as they slightly but definitely lower the agglutinin concentration and their preservative action is negligible

The effect of Infection

Contamination of the serum has a similar effect Deterioration of sera probably accounts for the cases of alleged change of blood group which have been reported from time to time

IV THE COST OF TYPING SERUM

The cost of typing serum has an important bearing upon the number of calls made for the universal donor

In Great Britain, as recently as 1935 the cost of typing serum

was almost prohibitive A pair of capillary tubes just sufficient to group one person cost 4s, that is to say 48s a dozen pairs The consequence of this was that many hospitals could not afford the expense of consistent grouping of their patients They therefore omitted it altogether and relied upon members of group O as universal donors, which threw a great strain upon this section of the service

The matter was investigated and arrangements were made by which high titre sera were obtained from selected donors in the London Blood Transfusion Service who were reserved for this purpose The sera so obtained is now supplied when required to a leading firm of manufacturing chemists who put it up in a suitable form for distribution The present cost is 6d a pair of tubes, that is to say 6s a dozen pairs, a reduction of 85 per cent, so that the plea of non possession of sera can no longer be accepted as a reasonable excuse for failing to have a patient grouped, even by the poorest hospital, although in my opinion the figure is still very much too high

With the marketing of reliable high titre sera at a reasonable price, there should be less disinclination to discard serum which has become stale and more inclination to do routine grouping both in antenatal clinics and before major operations

SUMMARY

1 The serum donor should be healthy, between the ages of 18 and 45, of either sex and normal stature, and he should be fasting at the time of withdrawal of his blood

2 Stock sera for typing purposes should in all cases be titrated because of the great variation in the titre of the agglutinin concentration amongst individuals of the same group

3 Inexperience is not a reasonable excuse for omitting titration as the technique is simple and can be quickly learnt without special laboratory training

4 The reading of the end point needs practice It is best to decide this with the naked eye It is no more accurate under the microscope and the latter takes longer

5 The minimum safe titre to be employed is a serum active in a dilution of 1 in 100

6 Sera devoid of prozone phenomena only should be selected

7 Potency is best maintained by selecting high titre sera in the first instance for stock purposes This is advised because titre value of strong and weak sera do not fall at the same rate The sera should be kept away from the light and in a refrigerator Contamination and the addition of preservatives slightly lower the agglutinin concentration

8 The value of concentrated and dried sera would appear to be greatest in tropical countries where fluid sera may lose bulk by evaporation

9 The widespread preparation and release of typing sera is desirable in the interests both of teaching and practice This is becoming more important in view of the increased use of blood transfusion as a therapeutic measure and becoming safer with the more general realization of the importance of marketing high titre sera only

10 The destination should be carefully noted by the distributors and ideally reminders sent when the time limit of potency is approaching

11 High titre—low priced—typing serum is an important auxiliary in the management of a transfusion service

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CHAPTER IV

BLOOD GROUPING TECHNIQUE

In many institutions it was noticed that an unnecessarily ponderous grouping technique was used

It started with the method of collecting the cells to be grouped As a rule this was done, after pricking the finger, by taking several drops of blood into a citrate solution and then centrifuging and washing in saline Sometimes the washing was repeated two or three times After mixing the typing serum and cells on a slide, the latter was occasionally placed in an incubator for a period of time varying from two minutes to two hours A microscope was then obtained, sometimes there was difficulty in focusing a fresh preparation Finally, the field in view, the interpretation was not infrequently tinged with uncertainty

The object of my investigations was to find the best means of simplifying this somewhat elaborate procedure, consistent with accuracy

Although there is really only one essential for accurate grouping, namely the use of high titre testing sera certain procedures will help to maintain accuracy to aid interpretation, to shorten the time taken to do the test, and in short make it more *practical*

Factors influencing the accuracy of blood group determinations will now be discussed

1 Medium on which the test is made

a. The actual mixing of cells and serum is best made *upon a white opal glass* tile This is smoother and more homogeneous than a porcelain tile, which owing to its granular surface, may give rise to a deceptive appearance under the hand lens simulating agglutination The white background makes the naked eye interpretation straightforward and the tile is easily warmed *It is the most practical bedside method*

Tiles with scalloped areas are not satisfactory, as the cells migrate to the bottom of the pool and distortion effects are produced under the lens by the sloping edges

A saucer or teacup turned upside down will serve very well in an emergency

The test was also seen carried out upon an ordinary glass microscope slide white glossy paper or cardboard, and in small test tubes All these variations can be interpreted by the naked eye aided by a hand lens

b The *slide* method is not advised as the interpretation is more difficult Furthermore if the microscope is used and a cover slip placed upon the fresh preparation the free migration of the red cells may be interfered with

To interpret with the naked eye the slide should be raised to the light and examined from below through its thickness or placed upon a white background

c A square of white glossy *paper* is used in Leningrad at the Blood Transfusion Institute with serum of groups A B and O upon it which has been allowed to dry A drop of saline is added to each to dissolve the serum and then a loopful of blood The possibilities of this method have not yet been fully explored elsewhere but they seem quite promising The serum is said to keep its agglutinin concentration very well

If a *card* with a white glossy surface is used the background makes the interpretation easy and if the mixture is allowed to dry the card can be filed amongst the permanent records (Paris Transfusion Sanguine d Urgence)

d With a *test tube* This method may be used with fluid serum or as in Vienna with dried serum Equal volumes of serum and cell suspension in saline are mixed in a small test tube and allowed to stand The tubes may be examined macroscopically a few minutes later or a drop of the mixture may be transferred to a slide and examined under the microscope

The reaction can be accelerated by centrifuging the tube for about three minutes After centrifuging the tubes are shaken a negative result shows as an even suspension of cells a positive when the cells remain clumped together The chief use for the method is when there are a *large series of cells to be grouped* as they can all be examined at the same time

2 Quantitative factors In most countries the unknown blood for typing is taken into saline or citrate producing varying dilutions This is probably the result of habit as at one time

it was considered necessary to wash the red cells first before putting them up with the serum since it was thought that with whole blood the associated agglutinins might interfere with the reaction This is now known not to be the case Frequently the dilution was excessive and when cells are added to serum in such low concentration agglutination if it occurs will be difficult to detect macroscopically

Whole blood should be added to the serum In this way by avoiding unnecessary dilution of the serum agglutinins the onset of the reaction will not be delayed and will reach its maximum in the shortest possible time *High titre typing serum will give an accurate result within two minutes*

This may appear to be an unsafe and dogmatic statement On the contrary I believe it to be a step towards greater accuracy and easier interpretation provided that

1 The typing serum is of known high titre being not less than 1–100
2 Whole blood is used and not blood which has been diluted by drawing it off into saline or citrate

The Medical Officer of the London Blood Transfusion Service has used this technique on approximately 10 000 donors and has found it consistently reliable My own experiences support this conclusion

3 Temperature factor *Incubation is unnecessary*

To inhibit the action of cold agglutinins which are inactive at body temperature incubation of the slide at 37° C has been advised In practice more often than not there are no facilities for incubation but fortunately incubation is unnecessary provided that in cold weather the tile &c is warmed before use

4 Time factor *It is safer to put a time limit to the reaction*

If the test is carried on for more than a few minutes *drying* occurs at the edge of the patch and simulates agglutination and the increased *concentration* in the centre of the mixture will cause rouleaux formation Between them these effects may mislead the observer and agglutination be decided upon where none exists

5 Method of observation *Naked eye or microscopic?* The use of the microscope in inexperienced hands is a frequent cause of mistakes particularly if a coverslip is applied Rouleaux

formation is more obvious under the microscope *and is easily mistaken for true agglutination*

Conversely the coverslip may prevent agglutination as pointed out by Paule Younge (1940) If a coverslip is used and very small drops of serum and cells as sometimes occurs in the direct compatibility test the liquid spreads out in a very thin film and the red blood cells are fixed between the two glass surfaces so that agglutination may be mechanically prevented

Naturally for a pathologist the o errors are reduced to a minimum but for those who use a microscope less frequently the naked eye method is the safest In addition it will be more practical to get into the way of coming to a decision with the naked eye as the grouping or cross test must often be done at the bedside and it is not always convenient to carry a micro scope around If in a given case the microscope is preferred the slide should be examined with the lower power first follow ing the well known histological axiom that if one is undecided under the low power one will be even more undecided when examining with the high power

6 **Sera used** In some countries—France Holland Hun gary Russia (1936)—as well as using A and B serum for typing O serum was used as well The reason for this was that if the titre of either or both the A and the B had fallen off, the O serum if potent would reveal this error In an institution where the use of stale A and B sera is possible there is no reason to suppose that the O serum will be potent

APPARATUS

Grouping will frequently have to be undertaken at the bed side and for this reason the simpler and more compact the apparatus the better A satisfactory method which can be carried out with a minimum of special apparatus and inter preted with the naked eye is described

Some form of cutting *needle* will be required such as a Hagedorn triangular needle or the ordinary surgical cutting needle Round bodied needles should not be used for choice but an ordinary sewing needle will make an excellent substitute in an emergency *A hand lens* with a magnification of ten times

will also be useful For transferring the unknown blood to be grouped, a platinum *loop* or a glass rod is preferable to a pipette which requires special cleaning and is easily broken A loop *made of stainless steel wire is better* than platinum as it is more rigid and does not break so readily It is conveniently cleaned by washing under a tap and drying with a cloth Two match sticks will do very well in an emergency

Summarized the apparatus and materials required will be

Typing sera A and B
Opal glass tile
Grease pencil
Platinum loop or its equivalent
Hand lens $\times 10$
Cutting needle

COLLECTION OF THE BLOOD FOR GROUPING

From the donor (Fig 8) By stabbing with a **needle** Favourite sites are the lobe of the *ear* and the terminal phalanx of a *finger*, and the *heel* of an infant The drop of blood so obtained is transferred by means of a platinum loop *directly* to the serum

From the *patient* (Fig 12) From a vein using a **hypodermic syringe** and needle

Since serum for cross matching has also to be obtained, it will be much quicker to collect the blood for *both purposes* at the same time and by a single puncture As the needle prick is only a slight one some small vein should be selected any obvious large vein being left undisturbed and reserved for the actual transfusion later on

Two drops of blood are expressed from the syringe one to each pool of serum, and the rest is quickly emptied into a small test tube The syringe should immediately be washed through with saline or cold water to prevent the plunger from sticking

When bedside grouping is inconvenient

(*a*) *Grouping at a distance*—e g by post

A few drops of blood are collected into 0 9 per cent sodium chloride containing 0 5 per cent sodium citrate

Washing is unnecessary A small test tube makes a suitable container

(b) *Grouping from clot*

In an emergency cells can be teased out of a clot and added directly to the typing serum

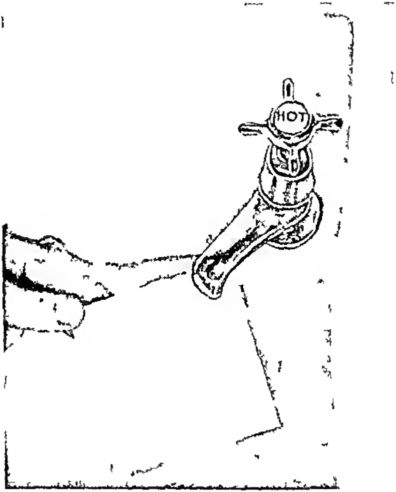


Fig 6 The t be is warmed nder the h t water tap a l l d

TECHNIQUE

I. Grouping with Stock Sera (Figs 6–10)

(i) The tile is warmed under the hot water tap to the extent of taking the chill off it, and dried

(ii) The tile is marked with a grease pencil with the letters A, B

(iii) The serum from the corresponding capillary tubes is blown out on the tile *to form a pool opposite each letter*

(iv) Enough *whole* blood to be typed—a small drop or two loopfuls—is now added to each serum pool to produce a definite pink coloration If the colour is very deep it is difficult to recognize the finer degrees of agglutination, and if the concentration of cells is too strong the agglutinins may be absorbed without producing agglutination

(v) The cells and serum are mixed with the platinum loop

(vi) The tile, held in the hand, is rocked from side to side This aids agglutination and tends to break up rouleaux Agglutination will usually be obvious without the hand lens and has the appearance of red pepper (brick dust) Characteristically the clumping is somewhat irregular as opposed to the even granularity of pseudo agglutination

(vii) The mixture should be examined with the hand lens in a good light, if there is any difficulty with the interpretation

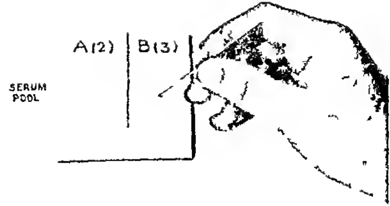
As a rule agglutination appears earlier with the B serum, and the clumping is coarser as the alpha agglutinin usually has the higher titre **High titre** *typing sera will give an accurate result* **within two minutes.** If, for any reason, there is still uncertainty at the end of this time, it will be much wiser

1 *To repeat the test rather than to prolong* it, bearing in mind the possibility of pseudo and cold agglutination If uncertainty persists, the investigator should

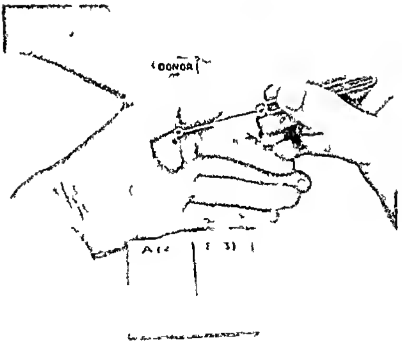
2 *Check the potency of the typing serum* (*a*) by examining the date when it was put up, and (*b*) by putting up the typing serum against known cells, for instance, the operator's own cells

3 If the test is being done in a laboratory the grouping should be repeated, using *stock cells* of A and B groups

4 If stock cells are not available—and they may not be in an emergency—a group O should be obtained and the transfusion started.



F 7 Th t p k mr s all l to the t le



F o 8 Wl le t x f s alded l rec ly to a l sert p ol The wire l x p
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l m to pr al re tl e drop f l l od

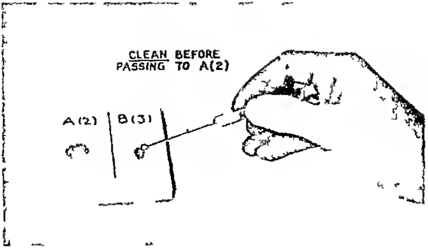

FIG 9 The cells and the serum are mixed

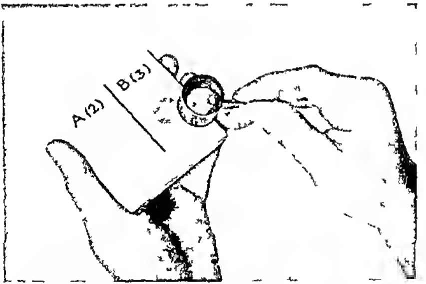

FIG 10 The tile is held in the hand and rocked from side to side to complete the mixing of the cells and serum Agglutination visible to the naked eye is seen in pool B The cells being grouped belonged therefore to a member of Group A.

II. Regrouping with Stock Cells

In grouping the members of a transfusion service it is imperative for the medical officer responsible for the blood group determinations always to group the donors on enrolment with stock cells as well as with stock serum

An additional safeguard will be to have the groups confirmed by an *independent opinion*

Every laboratory in which frequent blood group determinations are being made should have an available supply of A and B cells Such stock cells may be used for two purposes to check the potency of the stock laboratory typing sera from time to time and for blood grouping

In the rare cases of individuals with a low agglutinogen content giving a negative result with the stock sera the proper blood group will be revealed when such an individual's serum is put up against stock cells

The test will also give some idea of the potency of the individual s serum agglutinins

The method

After collecting into citrate the stock cells should be washed in normal saline, the supernatant fluid being discarded and a saline suspension of approximately 10 per cent red cells made These cells should never be kept for more than six days The test is done by mixing the stock cells with the unknown serum

III Grouping when no Typing Serum is available

(*a*) Compatibility can be determined by *cross matching* the patient s serum and the donor s cells—and omitting grouping altogether

(*b*) If the investigator knows his own group or that of any other person present who belongs to group A or B, it is possible to determine the four blood groups This may be done after separating the serum and cells of either an A or B and using them as standard reagents

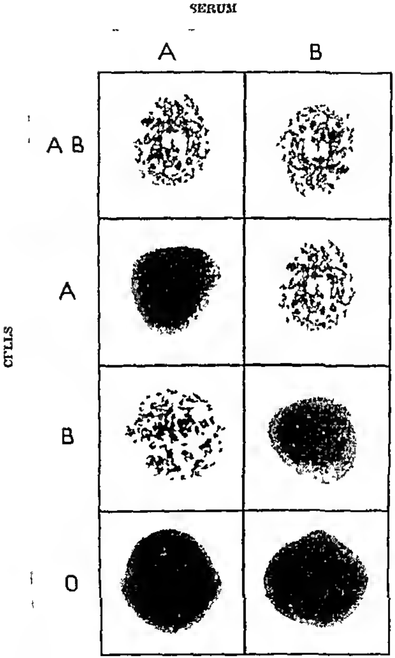

FIG 11 The agglutination reactions observed in routine blood grouping on the addition of red corpuscles to stock typing sera of groups A and B

Sources of Error

FALSE NEGATIVES

Stock typing serum—low titre

The typing serum may be of *low titre* either because it has become stale as a result of prolonged storage or because the original titre was never high enough. The titre is also interfered with by contamination by the use of preservatives and by storage in warm places.

Rare cases of false negative reactions

(*a*) Cells having a low agglutinogen content when added to stock serum may give a negative result. This will be shown up when the grouping is repeated with the individual's serum and stock cells.

(*b*) A serum having a low agglutinin content, as may occur in infants during the first year of life, when added to stock cells may fail to show agglutination. The agglutinogen factor is, however, normally developed so that the reaction when repeated with stock sera will show the group.

FALSE POSITIVES

Most errors are due to inexperience; they include:

Pseudo-agglutination

This effect, also known as **rouleaux** formation—owing to the arrangement of the red cells in piles like coins—is not uncommonly seen, especially if the observations are made with a microscope. Macroscopically it gives rise to a homogeneous granularity as opposed to the irregular clumping of true agglutination. The condition is a *concentration* effect and disappears *on dilution* with a drop of saline, which immediately distinguishes it from true agglutination. The phenomenon is most often associated with serum withdrawn from patients with a high temperature, a state of affairs which often produces an increase in the serum viscosity—possibly due to an increase in the serum protein. Pseudo-agglutination is most commonly seen in the acute infections, in pneumonia and in septicaemia. It is not a contra-indication to transfusion and does not influence the

frequency of reactions Pseudo agglutination apparently runs parallel with the blood sedimentation rate

Cold agglutination

The phenomenon of cold agglutination is very much commoner than is generally supposed Besides the iso agglutinins which determine the four Landsteiner blood groups there exist other agglutinins known as 'cold' agglutinins These agglutinins derive their name from the fact that they act only at low temperature When sera containing these agglutinins—and they are present in most normal sera—are mixed with human red cells at low temperatures (0°–5° C) agglutination of the red cells will occur irrespective of their group

Also if such a serum is mixed with the red cells of the *same individual* from which it is derived and the mixture is allowed to stand at ice box temperature (4° C) the cells will be agglutinated For this reason these cold agglutinins have also been called 'auto agglutinins'. When the individual's own cells are agglutinated by his own serum, it is termed auto agglutination, and when between serum and cells of different individuals, cold agglutination The active principle is absorbed by treatment with erythrocytes and is therefore of the nature of a true agglutinin (Gardner, 1936)

The reaction caused by auto agglutinins diminishes rapidly as the temperature is raised and is never demonstrable at body temperature, in contra distinction to pseudo agglutination Agglutination may, however, occasionally occur at *laboratory* temperature, and it is this type of case which has drawn attention to the phenomenon Bialosukma and Hirszfeld (1923) have explained this irregularity by showing that the same serum may contain different cold agglutinins coming into action at different temperatures or possessing, as they express it, different 'heat amplitudes' In Dyke's laboratory cold agglutination at room temperature has only been observed in the case of blood taken from severely anaemic patients, but it is exactly in this type of case that blood transfusion is most urgently needed

The practical application of this observation will come when cross testing the serum of such a subject with the cells of a prospective donor If it is remembered that it is in these

circumstances that cold agglutinins are most likely to act—owing to elevation of their heat amplitude enabling them to be active at room temperature—the blood of a donor which might otherwise have been thought to be incompatible may be used—an important consideration in an emergency

The incidence of the reaction is also said to be high in cirrhosis of the liver but although it may be accentuated under certain pathological conditions it is not itself to be regarded as pathological

Confirmation of cold agglutination. In cases where cold agglutination is suspected

1 The test should be repeated at 37° C at which temperature the phenomenon does not occur
2 The test should be repeated on a tile cooled under the cold tap or at ice box temperature when the reaction is intensified if cold agglutinins are present
3 The test should be repeated by mixing the individual's own serum and cells at low temperature Agglutination will occur if cold agglutinins are present

The significance of cold agglutinins and their method of action is not clearly understood Certainly there is something more than ordinary iso agglutination in these cases as not only will such a serum agglutinate its own cells but also those of group O which normally do not contain agglutinogen

Transfusion If the presence of cold agglutination is confirmed the question arises as to what is to be done when it comes to transfusing such a case If cold agglutination is to be regarded as a contra indication to transfusion then a number of unfortunate patients who exhibit this phenomenon will have to be left to their fate Since however these individuals do not agglutinate their own cells at *body* temperature by analogy one may assume that they will not agglutinate the cells of the donor and so cold agglutination need not be regarded as a contra indication to transfusion The incidence of reaction however is probably greater when cold agglutinins are present (p 79)

The use of the microscope

It has already been pointed out that the use of the microscope in inexpert hands is a frequent cause of false positive results, as rouleaux formation is more obvious and is easily mistaken for true agglutination

Waiting too long for result

Another not infrequent cause of a false positive reaction is due to the observer's inability to make up his mind within a short time As has been mentioned elsewhere, the longer one waits the more difficult it is to come to a decision owing to the concentration of the mixture and drying effects *It is always better to repeat the test rather than prolong it*

Sub-groups

The *cells* from an individual with accessory agglutinins give a normal reaction with typing sera that is to say, adventitious agglutinins do not interfere with the interpretation of the grouping test

The *serum* of these individuals, however, when added to stock cells or in the cross match tests, will cause agglutination, but only if the corresponding adventitious agglutinogen is present in these cells—a rare coincidence

In practice the important point to bear in mind is that these irregular reactions can be excluded by the simple expedient of *cross matching before each transfusion*

SUMMARY

1 *Accurate grouping depends upon*

(i) The use of reliable reagents that is to say, *high titre* typing sera

(ii) The mixing of *undiluted* blood and undiluted serum

(iii) Carrying out the test on a medium *opal glass tile*, which is easily warmed to body temperature and provides a suitable background—white and homogeneous—to aid the interpretation

(iv) A *macroscopic* method of interpreting the result

(v) Establishing a *time limit* for the reaction

2 Ideally the potency of the typing serum should be confirmed on each occasion before use by putting it up with known A and B cells

3 Whenever possible the grouping as determined by stock sera should be confirmed by regrouping with stock cells or by an independent opinion

4 Sources of error are usually due either to

(i) The use of *impotent* typing sera.

(ii) *Pseudo-agglutination* a concentration effect which disappears on dilution with saline and re examination of the fresh preparation without a cover-slip

(iii) *Cold agglutination* omitting to warm the tile so that agglutination in the cold may occur This disappears on warming the tile to body temperature and is accentuated by cooling of the tile It is confirmed by agglutination (in the cold) of the individual's own cells by his own serum.

(iv) The use of the microscope

(v) Prolonging the decision of the result of the reaction

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CHAPTER V

THE DIRECT COMPATIBILITY TEST

Definition. In the Direct test, sometimes called Cross matching, Cross grouping, or *Cross agglutination*, the compatibility of the two bloods concerned is determined by putting up the patient's agglutinins against the donor's agglutinogens. The basis for compatibility is the agglutination reaction and not the haemolytic reaction since it has been observed that when incompatibility is present agglutination precedes haemolysis. The test is made by mixing the patient's serum and the donor's cells on a glass slide or tile. Dyke of Wolverhampton (1938) believes the test to be so important that he says 'preliminary knowledge of the blood groups of the Donor and Recipient is not necessary, *what is essential is evidence that the serum of the Recipient be incapable of agglutinating the red cells of the Donor*'.

The **serum** *of the patient* rather than that of the donor is taken, since *in vivo* it will be the agglutinins in this serum which will be quantitatively the most numerous and in titre the most potent. They will therefore dominate the direction in which a reaction if it occurs will tend to go.

The Importance of the Direct Test

The direct test should be observed whenever possible since it will expose:

1. Grouping Mistakes

In cases of incorrect grouping of donor or recipient the mistake will be revealed. In this respect the direct test acts as a check on the potency of the typing serum, and as a control upon the original interpretation of the grouping.

2. Intra-group incompatibility.

Two individuals, although they may be of the same group, are not necessarily compatible. When incompatibility occurs between bloods of the same group, it is due either to the interaction of *sub groups* or, rarely, after *multiple transfusions*, to the formation of additional agglutinins. These are contingencies which the determination of compatibility by grouping alone would fail to unmask.

More donors are rejected as incompatible from group A than from any other, owing to the presence of sub groups—and for the same reason a higher percentage of reactions occur with this group than with any other The same conditions hold for group AB, which is also divisible into sub groups but owing to the rarity of this group the occasions for transfusions are very infrequent

3 Telephone Mistakes

Mistakes may occur in the following circumstances

(i) *Request for the wrong group* If the donor has been summoned *by some one other than the individual responsible* for the blood grouping for example by a telephone operator, a nurse or another doctor In these circumstances mistakes in transmitting the message sometimes occur

If knowledge of the group of the patient depends upon *a verbal message* from a third or (fourth) party not responsible for the groupings for instance I had experience of a case recently in which the patient s medical attendant obtained a pathologist to do the grouping The pathologist in due course reported the blood group to the doctor who then asked a surgeon over the telephone to do the transfusion naming the patient s group A donor of this group was obtained but a cross test showed obvious incompatibility the donor and recipient being of different groups

(ii) *Mixing of donors* Not infrequently more than one donor may be attending the same hospital at the same time and it has happened that they have been mixed

4 If the donor and recipient have been *grouped by different individuals* i e using different typing sera and technique

5 If the patient is in a state of *advanced anaemia* because in such circumstances every precaution must be taken to avoid a reaction The greater the anaemia the more important is the question of ideal compatibility

The reverse cross test

The agglutinins in the serum of the donor might be expected to react with the recipient s corpuscles How is it then that any

transfusion is safe without this test being made as well? The reason is that in same group transfusions in which the average transfusion is 500 c c which amounts to one tenth of the total blood volume the incoming serum is so diluted (ten times) that these agglutinins are rendered ineffective and so may be ignored This does not apply when the donor is of a different group (see p 45)

Frequency of the direct test

It is difficult to estimate how often the direct test is employed in this country In an attempt to find this out ten of the more experienced members of the London Blood Transfusion Service were questioned They had given 303 transfusions between them i e an average of approximately 30 each Their general impression was that cross matching was only performed in about one third of transfusions In certain continental countries and some of the States of America it is omitted altogether Elsewhere it is done in about the same proportion of transfusions as in Great Britain

In no circumstances can the direct mixing of a drop of whole (or citrated) blood obtained from the donor and from the recipient be regarded as an adequate test for compatibility In this way no account is taken of the dilution of the serum or of the concentration of the cells (Gardner 1930)

THE COLLECTION OF THE PATIENT S SERUM

The patient s serum is most conveniently collected *at the same time* as he is grouped By using a hypodermic syringe and needle enough blood can be collected in a single venepuncture for both tests

If the serum is collected by pricking the lobe of the ear or the finger apart from the extra prick it often happens that only a minute quantity is produced from which it is difficult to obtain even a loopful of serum the *intravenous* method is quicker and altogether more practical

If the blood sample can be left for twenty minutes—preferably in a warm place such as a pocket—a sufficient yield of serum will be obtained and in the meantime other details connected with the transfusion may be attended to

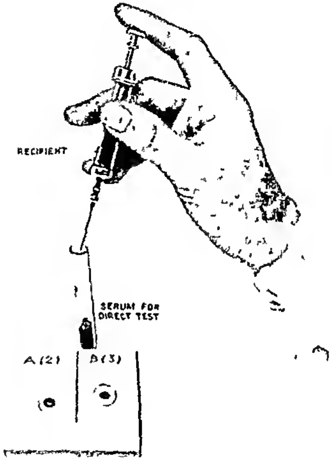

FIG. 12. Serum for the direct test by a hypodermic [illegible] syringe from a vein. One drop is expressed on to each serum pool for the blood group determination, the remainder is emptied into a small dry test tube. This blood clots and expresses a clear serum.

It will be found that the serum of anaemic cases separates most rapidly.

The serum should not be left in *contact* with the clot for more than twenty four hours.

No centrifuging

To accelerate the separation it has been suggested that a portable hand centrifuge should be used Apart from its clumsiness it is not always satisfactory to centrifuge the blood immediately after its withdrawal Serum rapidly separated is often not fluid but clotted—due to retained fibrinogen

Multiple transfusions

Individuals who are to receive more than one transfusion must be re cross matched with freshly collected recipient serum before each transfusion At the time of the second or third transfusion it is useless to cross match with serum collected from the patient before the first transfusion and stored for subsequent use

Serum collected for the cross match test should be kept for twenty four hours—in case there is a reaction following the transfusion—but after that it is of no use and should be discarded

TECHNIQUE OF THE DIRECT TEST

Procedure

The opal glass tile is used and warmed first as when grouping A few drops of the patient s serum are now put on the slide and enough of the donor s blood is added—usually two loopfuls will be enough—to produce a strong pink coloration and the two are thoroughly mixed The tile is rocked from side to side and if compatible no change will take place Incompatibility will show as agglutination

How long to wait for a result Very wide differences of opinion have been expressed on this matter and cases have been quoted of agglutination reactions which have only been detected after prolonging the cross test for several hours One cannot help thinking that some at least of these may have been cases of wrong grouping and that the time would have been better spent in checking the titre of the typing serum or regrouping the participants

In practice it is unwise to wait longer than **two minutes** After this drying effects around the edges confuse the issue and concentration in the centre produces pseudo agglutination

If at the end of two minutes there is no evidence of agglutination the bloods are for all practical purposes compatible. An agglutinin of a titre high enough to do any harm will bring about agglutination in less than this time.

If definite agglutination occurs then there is incompatibility, and the donor must be rejected and the grouping repeated.

If uncertainty exists at the end of two minutes it will be better to repeat the test rather than prolong it, *bearing in mind* pseudo agglutination (p. 34) and agglutination in the cold (p. 35).

Even after this one may occasionally be undecided; the urgency of the case will direct one's line of action. It may be convenient to reject the donor and obtain another if this can be done at short notice, or it may be quicker to regroup both donor and recipient and rely on these findings. If there is any reason to doubt the potency of the typing serum used for the grouping, this should be checked by putting it up with known A and B cells. If these are not available and the donor's group or the operator's own group is known with certainty, their cells can be used instead, unless both happen to belong to group O.

False positives

Far and away the commonest cause of apparent incompatibility is *pseudo-agglutination*, followed next in frequency by *cold agglutination*. The former disappears on addition of a drop of saline, the latter on warming the tile.

True positives

These are rare and are due either to *incorrect groupings* or the presence of *sub groups*. Incompatibility due to the presence of sub groups most commonly occurs between individuals belonging to group A. Such sub group reactions are peculiar to the two individuals concerned. They are probably less than 1 in 10 000 transfusions.

The value of the test when no typing serum is available

In an emergency, if no typing serum is available, the only rapid way of determining the suitability of a donor will be by the direct cross test. If this is satisfactory it will be safe to use the donor, though it will be wise to give the injection slowly to be on the safe side.

THE REVERSE CROSS MATCHING TEST

In the reverse cross test the donor s serum and the patient s cells are mixed Considerable controversy has arisen as to the advisability of doing this test as well as the direct cross test as a routine before each transfusion It is generally unnecessary in this connexion The argument is that an incorrect grouping may not be detected by the direct cross test if the agglutinins of the patient are present in his serum in low titre It is said *quite reasonably that if the test is reversed the error will almost* certainly be exposed

But this is attacking the problem from the wrong angle Instead of elaborating an additional test to expose a weakness in two preliminary tests (the grouping and direct cross test) it would be better from the beginning to teach the importance of employing high titre testing serum and of regrouping with stock cells than of how to expose the mistakes due to stale or weak sera If one is to regard a recipient s serum with a low titre of agglutinins as a danger then the value of the ordinary cross test is immediately challenged and the commonly performed emergency compatibility test between a patient and a *relative would have to be rejected Since this is frequently* performed and no fatal cases can be traced to this method of deciding compatibility it may be regarded as reliable Furthermore if the agglutinins are not present in high enough titre to cause agglutination in the direct cross test it is highly improbable that they will cause any reaction when the actual transfusion is given even though the blood be of a different group

Transfusion is still mainly an emergency procedure and to introduce another control as well as the direct cross test is going to overburden the transfuser and add a test of limited value which is quite impracticable in the average case

The reverse cross matching test *in transfusion of the Universal Recipient (group AB) from the so called Universal Donor*

From a practical point of view the only occasion on which double cross matching need be practised is when there is a possibility of *a double reaction* between two agglutinins and two agglutinogens These conditions only exist *when a group AB is*

receiving a group O (containing α and β agglutinins) (Fig 13) This is the most dangerous combination possible, and a severe reaction can occur even if the incoming agglutinins are of comparatively low titre, due presumably to a summation effect of the double reaction

By including the reverse cross test in these circumstances an indication of the titre of the incoming agglutinins can be obtained

The test will naturally produce agglutination between the agglutinins (alpha and beta) in the universal donor's serum and the A and B agglutinogens in the recipient's cells but the degree of clumping produced varies with the titre of the donor's agglutinins A high titre O will produce rapid and extensive clumping a low titre O a slower and finer clumping

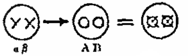

FIG 13

SUMMARY

1 The direct test should always be carried out unless there is some good reason for omitting it such as great urgency

It is not safe to omit the test as a routine because

(*a*) Mistakes in grouping or in providing a donor of the required group will otherwise go undetected

(*b*) Individuals even though of the same group, may be incompatible (sub group reaction)

2 Enough blood should be collected for the grouping *and* cross agglutination test at the same visit This is best done by intravenous puncture

3 If the serum is required in a hurry it will separate more quickly by leaving the blood so obtained to clot rather than centrifuging immediately after collection

4 The test should be performed as when grouping, upon a warmed opal glass tile using whole blood and undiluted serum, and observing with a hand lens for not longer than two minutes

5 If there is doubt about interpreting the result of the cross matching it will be well to bear in mind the possibility of pseudo agglutination agglutination in the cold, and true incompatibility The first two points will be cleared respectively by

dilution and by warming If true incompatibility is suspected, wrong grouping or a sub group reaction is probably the explanation If the former is the more likely, the patient and donor should be regrouped, but the potency of the typing serum should be confirmed first If a sub group reaction is the more probable the donor should be rejected and another obtained

6 The commonest cause of apparent incompatibility is pseudo agglutination

The commonest cause of *true* incompatibility is *erroneous primary grouping*, and not a sub group reaction

7 The value of the test when no typing serum is available is pointed out

8 Reverse cross matching is advised in transfusions of group O blood to universal recipients, because of the danger of a double reaction

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CHAPTER VI

THE UNIVERSAL DONOR

THE ABUSE OF THE UNIVERSAL DONOR

The indiscriminate use of members of group O as universal donors may be challenged in two directions namely in the danger to the recipient and its danger to the organization of a service

THE HIGH TITRE OR DANGEROUS UNIVERSAL DONOR

There is still a considerable difference of opinion as to the margin of safety present when employing a group O as a universal donor In England and some other countries the use of this group for administration to groups other than its own is regarded as unsafe and only justifiable in emergency states.

In certain European countries, on the other hand, it is the practice to enrol as members of a service individuals belonging to group O only

In France, where group O donors are almost exclusively used, I inquired the group of the recipient at a transfusion and was answered, 'We do not know the patient's group, therefore we cannot give him the wrong group' The teaching was that desire for knowledge of the recipient's blood group was a form of dangerous curiosity, and furthermore unnecessary

The argument in that country in favour of the general use of the universal donor was upheld on the following grounds. Firstly, that it was in fact a more rational procedure in view of our present incomplete knowledge of the sub groups, secondly that by omitting the grouping of the recipient, the possibility of mistaken grouping in any given transfusion is immediately reduced by half This omission was justified by the claim that in their practice the universal donor could be safely used for all recipients who were not gravely anaemic

In addition, the method had the advantage that it was quicker because the recipient did not require grouping, that it was safer in the hands of the inexperienced because the donor supplied by the transfusion centre was always a certain group O, and that it simplified the organization because only one group had to

be recruited, and that the group which was present amongst the population and therefore the applicants in the highest proportion

This point of view is certainly an interesting one and if the safety of the universal donor was an established clinical fact the advantages would appear to outweigh any theoretical objections From the point of view of a voluntary service however, the use of universal donors only would put such a strain upon this group that even in the largest cities the demand would almost certainly exceed the supply if the present frequency of service (*four times a year*) *was to be maintained* In professional services presumably this difficulty does not arise as donors serve as often as once a month

It is only fair to note that no fatality has occurred in the experience of the Transfusion Sanguine D Urgence in Paris which supplies universal donors for 6 000 transfusions a year and of Brines (1930) in America (Detroit) who quotes 4 000 transfusions mostly with universal donors without a fatality

Coca of the Transfusion Betterment Association in New York (the Bureau for the supply of professional donors to New York City) reports 418 transfusions by universal donors to patients of other groups between 1931 and 1937 without a fatality The average volume transfusion given in this group of transfusions was 500 c c but the iso agglutinating potency of the donors used had been estimated and no high titre group O s were used (Coca 1938)

It must be mentioned that almost all the transfusions in the first two series—Paris and Detroit—were of whole blood obtained from professional donors and given by the direct method This combination of circumstances usually means that not more than 300–400 c c is given (partly because more blood means more money and partly because technical difficulties may put an end to the injection) Now it is well known that *death from the transfusion of incompatible blood rarely occurs when less than 300 c c is transfused The comparatively small* amount of blood transfused may thus be the explanation of the absence of fatalities in this particular series of cases In spite of these figures it was the opinion of the International Congress at Paris in 1937 that *the indiscriminate use of the universal donor was dangerous* The reasons for making this statement

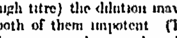
will now be considered and it will be seen that they are partly upheld by a study of the quantitative serological factors involved and partly by the results of clinical experience

The Recipient in relation to Donors with sera of high titre

The teaching that the incoming serum is so diluted by the blood of the recipient that the agglutinins in this serum are rendered inactive can only safely be applied to transfusions in which *both participants are of the same group* From titration of sera it is known that an agglutinin may be active in a dilution of 1 400 yet no such comparable dilution takes place when a high titre serum is introduced into the blood stream When an antagonistic agglutinin is introduced e g when using group O as a universal donor to some group other than its own or when transfusing a group AB with some group other than its own and particularly when *two* such agglutinins are present in the incoming serum (and if in addition they are of high titre) the dilution may not be nearly sufficient to render both of them impotent (This is why identical group transfusions are always advised) In such circumstances interaction between the donor s serum and patient s cells will occur Such conditions are present if group O (IV) containing alpha and beta agglutinins is used as the universal donor to any group other than its own that is to say AB (I) A (II) or B (III) particularly if in such a case the incoming donor s serum is of high titre

'Universal' donor to group AB

If we consider the different blood groups it is clear that *the most dangerous set of circumstances* will be present when both the alpha and beta agglutinins of a group O donor are of high titre and the blood is given to a group AB with well marked A and B agglutinogen factors In such a case the



αβ AB

Fig 13

dilution of the incoming serum may only be slight and a severe reaction may take place

The practical outcome of this is that if an AB cannot be found for an AB it is safer to transfuse with an A or a B—in which

case only one incompatible agglutinin is introduced—except in the unusual circumstances of a known low titre O being available as the donor

Probably the reason why disasters are not more commonly reported is because of the rarity of transfusions to group AB patients who form such a small proportion of the population It has been advised elsewhere (cross matching) that when an AB is to be transfused by an O, the reverse cross test should be employed

An example of a severe haemolytic reaction following the use of a 'Universal' donor to a group AB recipient is reported by DeGowin (1937)

A woman aged 25 developed post partum fever following a medical induction of labour *It was decided to give a blood transfusion* The patient was found to belong to group AB No donors of this type were available at the time so her blood was cross matched with that of a group O donor No agglutination or haemolysis occurred in the mixture of the donor's corpuscles and the recipient's serum but the donor's serum seemed to produce prompt agglutination and haemolysis of the recipient's cells In spite of this reaction the patient was transfused with *citrated blood by a gravity method When 125 c c of blood had been* given the patient complained of a feeling of constriction in the chest and severe shortness of breath The administration of blood was promptly discontinued She became intensely cyanotic and dyspnoeic A rigor occurred and the temperature rose to 106 2° F , the pulse rate was 140 and the respiratory rate 44 per minute Two hours after the transfusion the recipient's blood serum was found to be tinged with haemoglobin and the Van den Bergh reaction gave a biphasic response There was no haemoglobinuria or oliguria The symptoms persisted only a few hours and by the next day she felt well

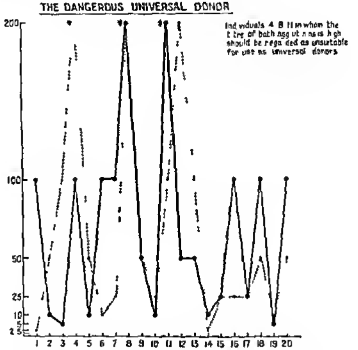
Investigation The donor's blood was retyped and found to belong to group O The recipient's blood was also retyped and established as group AB *On titrating the donor's serum the alpha agglutinin was potent* in a dilution of 1 in 80 and the beta agglutinin in a dilution of 1 in 12

'Universal' donor to group A.

If a group O with a high titre alpha agglutinin—the more usual finding—is given to a group A interaction may occur between the alpha agglutinin and the agglutinogen factor A present in the cells of this group Whereas such a group O will be unsafe to give to a group A, it will probably not cause a reaction if given to a B

'Universal' donor to group B.

The same argument holds good for a group O with a high titre β agglutinin which can safely be given to a group A but not to a B In practice, however, the titre of the O is rarely known so that it will not be possible with a given group A or B recipient to say whether it will be safe to use it It is better therefore to avoid the combination if possible



RANGE OF VARIATION OF THE α ( ) AND β(—) AGGLUTININ TITRE IN 20 CONSECUTIVE INDIVIDUALS OF GROUP O

Fig 14 (Riddell and Harwood)

The more *anaemic* the patient, the fewer will be the number of the circulating erythrocytes All the more serious then will be the result of the destruction of any of these cells, should a reaction occur since the quantitative reduction of erythrocytes will be proportionately greater than in a less anaemic person and will add to the ill effects of the haemolysis

Variation of agglutinin titre

In order to show that a variation exists between

(i) the titre of the alpha and the beta agglutinins present in any given group O,

(ii) the titre of the alpha agglutinins in different members of group O,

(iii) the titre of the beta agglutinins in different members of group O,

a series of members of group O were obtained by grouping and then double titrations were carried out The results may be seen in the accompanying chart (Fig 14) It will be seen that

(i) the titre of the alpha or beta agglutinin or both may be very high,

(ii) the titre of the alpha agglutinin is more often the higher of the two

Similar observations have been recorded by Brewer (1937) and Kettel (1930)

The practical outcome of these observations is that group O donors

(i) in whom both alpha and beta agglutinins are present in low titre should be reserved for emergency calls to any group and may be regarded as safe universal donors

(ii) in whom both alpha and beta agglutinins are present in high titre should be reserved for members of their own blood group and should be regarded as 'dangerous' universal donors Coca found the incidence of dangerous universal donors to be 3 per cent in 350 prospective group O donors (Coca 1931)

(iii) in whom only the alpha agglutinin is present in high titre should be regarded as dangerous for group A and AB, but 'safe' for groups B and O

(iv) in whom only the beta agglutinin is present in high titre can be given with safety to group A as well as group O, but should be avoided when transfusing to group B or AB

II THE DISORGANIZATION OF A BLOOD TRANSFUSION SERVICE

Even if the ideal measures just discussed can be carried out, and they are not necessarily councils of perfection, there is yet

another aspect of the indiscriminate use of the universal donor This is the effect such an unequal demand has upon the efficient running of a transfusion service It has been seen (Organization) that from this point of view, the *disproportionate calling up* of donors results in the overworking of one section of a service and the under employment of the remainder

Inquiry into the cause of disorganization of a service

When holding an inquiry into the cause of disorganization of a transfusion service *the first point* to determine will be to find if the fault lies with the hospital or the service The former may be demanding an excessive number of group O s or the service may be supplying group O s even when they are not being asked for them The latter may occur in a lax service if members of the correct group are not easily available and can be remedied by insisting on donors being called in strict rotation

In connexion with the excessive demand for Group O's the first line of investigation will be to see if a long run of calls for this group can be traced to *any particular hospital* On inquiring at such an institution the usual explanations given in their order of frequency are that there was no time to do the grouping that there was no pathologist available or that there was no serum

With regard to the question of insufficient time although this may be true of a few exceptional cases it cannot be applied to the majority in which a possible blood transfusion can usually be anticipated and the grouping done on admission It is more often than not another way of saying that the eventuality had not been thought about or that a chance was taken knowing that a service donor could be obtained at the last moment if necessary

Refusal to supply the universal donor if grouping has not been done is the prerogative of a voluntary service in these circumstances This measure had to be instituted in London in 1929 when a crisis was reached in the demand for the universal donor The effects of this ruling have been far reaching so that the present demands for the universal donor are little in excess of the normal percentage of the population proving the contention that the universal donor was previously being demanded unnecessarily (Fig 15)

With regard to a pathologist a voluntary organization in

view of the increase in frequency of blood transfusion and its own gratuitous services, has a right to expect that some member of the resident staff even in the smallest hospital shall be familiar with the technique of grouping

In connexion with the possession of stock typing sera, the

BLOOD TRANSFUSION IN THE LONDON AREA 1928 — 1938

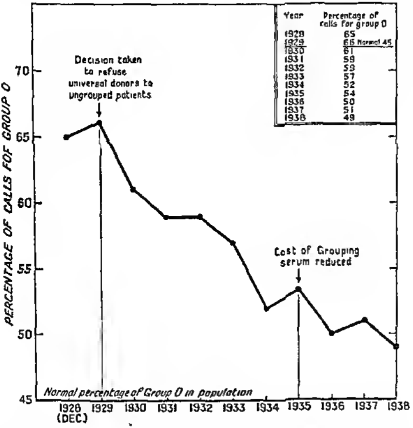


FIG 15 The graph shows the disproportionate demand that was being made for group O donors in 1929 and the effect of the decision then taken

cost of this in Great Britain before 1935 was so high that many of the smaller institutions could not afford to purchase it, and the natural outcome of this was to ask for a universal donor Since, however, the cost has recently been very much lowered, this demand is no longer excusable.

Occasionally it is found that none of these rules is being

transgressed and some difficulty is found in explaining the position, the hospital authorities firmly asserting that grouping is being conscientiously carried out on each patient In such a case it will be well to suggest that *the potency of the typing sera* used be investigated On several occasions it has happened that hospitals have been using impotent typing serum not necessarily because of prolonged storage, but sometimes due to a low initial titre which has rapidly worn off In these cases the patients were all being grouped as O s as the type testing serum had lost its agglutinating power

SUMMARY

Donor

1 The indiscriminate use of group O s as universal donors is dangerous

2 In a real emergency it is justifiable to use the universal donor for any group A severe reaction may occur, but a fatality is unlikely

3 If the transfusion is less urgent and there is time to obtain a donor the corresponding group should always be given

4 If this is not possible and a universal donor only is available it will be relatively safe to proceed after the usual cross matching test with a recipient of group A (II) B (III) (and of course O (IV)—the same group) because only one incompatible agglutinin is being introduced

5 If the *recipient* is group AB (I) (3 per cent), however, the use of a group O donor should be avoided if it is at all possible, owing to the risk of a double reaction

6 If the use of an O for a group AB recipient is unavoidable, it will be wise to mix the recipient's cells and the donor's serum first (reversed cross matching)

7 In transfusing a donor of group O to the different blood groups the order of safety will be

To a recipient of group O (safest)
" " of " B
" " of A
" " of " AB (most unsafe)

8 It is suggested that the infrequency of fatalities following

the use of group O as the universal donor in whole blood transfusions is due to the comparatively small volume of blood transfused The number of severe reactions has never been reported

9 In transfusing a recipient of group AB—the choice of donors in their order of safety will be

From a donor of group AB (safest)
" " A
" " B
" " O (most unsafe)

B is placed after A, as the alpha agglutinin present in group B is more often of higher titre than the beta agglutinin present in group A

Organization

10 It is suggested that a voluntary as opposed to a professional service would have great difficulty in maintaining a panel of group O donors only, large enough to meet the average demand

11 Ideally all group O recruits should have their sera titrated and those in whom both alpha and beta agglutinins are of low titre should be reserved for answering emergency calls and indexed separately, the remainder to be used for transfusions to members of their own group (O)

12 If the term 'universal donor' is to be retained it should be applied only to those *individuals in whom the alpha and beta* agglutinins are known by titration to be present in low concentration

13 Excessive use of the group O donors will disorganize a service and destroy its fundamental 'emergency' character

14 Over use of the universal donor can be avoided by

(i) The hospital authorities who should teach and encourage anticipatory grouping and should ensure familiarity with the *technique of grouping among the resident staff*

(ii) The Central Office of the service, by refusing calls for universal donors unless satisfied that the case is one of true emergency, and by calling up donors in strict rotation

(iii) Institutions and commercial houses placing typing sera on the market at as low a cost as possible

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CHAPTER VII

THE PHYSIOLOGY OF THE BLOOD GROUPS

THE QUESTION OF NOMENCLATURE

KARL LANDSTEINER in 1901, while working in Vienna, published his discovery of three blood groups, naming them A, B, and C Landsteiner at this time found no case in which the agglutinins were both absent and the agglutinogens both present A year later (1902) von Decastello and Sturli, the latter a pupil of Landsteiner, discovered the fourth and rarest group (group I Moss and AB International) In 1907 this work was corroborated by Jan Jansky, who *suggested a classification*, but unfortunately published his article in an obscure Czech journal (the only copy of which in this country is in the University Library at Cambridge) In 1910, W L Moss of Johns Hopkins Hospital, Baltimore, described his own confirmation of the existence of the four blood groups and suggested an alternative nomenclature Moss was unaware of Jansky's paper until after he had completed his own research Owing to the wide publicity given to Moss's work his suggested classification became the more generally used

The two notations chosen by the respective workers differed in that the numbering of groups 1 and 4 was reversed the other groups remained the same, so that group 1 Jansky corresponded to group 4 Moss and group 4 Jansky corresponded to group 1 Moss

It is not surprising that some confusion resulted from this, both in the practice of blood transfusion and in the literature In order to obtain uniformity of nomenclature the matter was discussed before the Public Health Committee of the League of Nations by the Commission for Standardization of Sera

It was there suggested that the four blood groups should be renamed by *lettering so as to give some scientific information* about the blood group to which each was appended It was suggested that these letters should be used to indicate the agglutinogen content of the cells of each group The classification on the basis of the agglutinogens was chosen because the agglutinogen is the dominant hereditary factor This classification

and the corresponding numbering of the Moss and Jansky grouping are compared in the following table

Jansky	IV	II	III	I
Moss	I	II	III	IV
International	AB	A	B	O

In the course of travelling the general impression was that the International Nomenclature was gaining ground particularly in Europe On the other hand in New York at the central offices of the transfusion bureau it was noticed that the telephone operators first question on receiving a call for a donor was Moss or Jansky ? In 1929 it was computed that about 80 per cent of hospitals in the U S A were using the Moss plan

In England the International Nomenclature is gradually being adopted It is the official nomenclature of the London Transfusion Service which serves some 400 hospitals

It is possible that a more widespread use of the international lettering could be obtained if the central bureaux of the various Organizations were to insist upon its use by hospitals when telephoning for a donor

It is to be hoped that the Moss and Jansky notations will gradually disappear from scientific publications wherever else they may be used

Summary It is suggested that the International nomenclature should be generally adopted because

(i) From a scientific point of view it is more rational
(ii) From a clinical point of view it is safer
(iii) From a terminological point of view it is simpler

THE PHYSIOLOGY OF THE BLOOD GROUPS

The physiology of the blood groups arose from observations by Landsteiner that the cells of one person were frequently agglutinated by the sera of others This phenomenon did not occur at random but appeared to divide the small series he examined into three groups observations on a larger number established the existence of an additional group To account for these observations Landsteiner postulated the presence of

agglutinins in the serum **reacting with** *specific agglutinogens in* the cells This supposition was confirmed by absorption experiments which showed that the active principles were true agglutinins, that they were truly specific to the corresponding

Percentage distribution	GROUP	CORPUSCLES Agglutinogens		SERUM Agglutinins		FORMULA
4	AB	AB		O(*absent*)		OO ABo
43	A	A	O	β	X	OX $A\beta$
8	B	B	O	α	X	OX $B\alpha$
45	O	O(*absent*)		$\alpha+\beta$		XX $O\alpha\beta$

FIG 16

agglutinogens, and that apparently agglutinin and agglutinogen could not occur in the same blood The separate identification and isolation of these groups came later (Fig 16)

For practical purposes the existence of two agglutinogens and two agglutinins is enough to account for all the phenomena of haemagglutination It is evident, however, that the possible combinations of these four factors is by no means limited to the formation of four groups Sixteen mathematical possibilities are in fact possible, and after subtracting biological impossibilities—namely the coexistence of homologous agglutinins and *agglutinogens—there remain nine possible combinations Of* these the four Landsteiner groups are the most commonly found the remaining possibilities are occasionally met with They are usually present as defective blood groups, that is to say either the agglutinin or the agglutinogen factor is missing Thus an individual may possess A cells but no agglutinin—

A o—or O cells and only one agglutinin—O β (Whitby and Britton 1937)

The interaction between the serum and cells of each of the

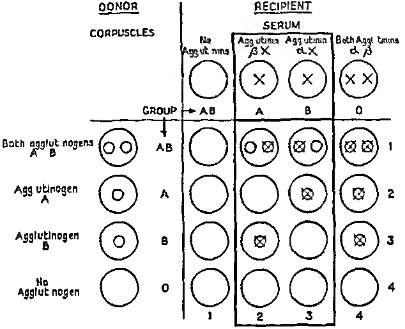

Fig 17 A table to show the agglutination reactions that may occur when the corpuscles of the different groups are added to the serum of the different groups. The central part of the table shows the agglutination reactions that occur in routine blood grouping. Agglutination is illustrated as a cross X superimposed upon a circle O

four groups is seen in the above table (Fig 17) To make the table of more practical interest the serum may be regarded as a recipient s and the cells as a donor s since from a transfusion point of view this is the important interreaction

Diagrammatically this table may be represented as follows

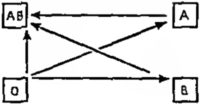

Fig 18

From the table and diagram it is seen that

A Recipient of group AB can receive blood from all 4 groups and for this reason is called the universal recipient.
" " A can receive blood from his own group and from group O,
" " B can receive blood from his own group and from group O
" " O can receive blood from his own group only,

and that

A Donor of group AB can give blood only to his own group,
" " A can give blood only to his own group and group AB,
" " B can give blood only to his own group and group AB,
" " O can give blood to all four groups and is therefore called the universal donor

It is clear that the foregoing conditions take no account of the possible agglutination of the recipient's corpuscles by the donor's serum. Yet if the donor's serum is of high titre, the dilution it undergoes may not be sufficient to render its contained agglutinins inactive, and an agglutination reaction may occur. This is most probable when a group O donor is used for a group AB recipient (p. 50).

If Fig. 17 is reconstructed and the incoming serum agglutinins assumed to be of high titre, it will be found that only identical group transfusions are absolutely compatible.

The reason why these reactions do not always take place is because the incoming serum, if it is of low titre, is so diluted by that of the recipient that it is no longer capable of causing agglutination. In practice, however, we do not usually know the agglutinin titre of the donor's serum so that when possible it is safest to use a donor of the same group as the recipient (see the dangerous universal donor).

Blood grouping.

From Figs. 11 and 17 it will be realized that the blood group of an individual can be determined by mixing the unknown corpuscles to be typed with sera of groups A (II) and B (III).

From these tables it will be seen that if the unknown corpuscles are agglutinated by

Both A and B sera, the individual belongs to group AB
A serum but not by B serum, the individual belongs to group B
B „ „ A serum, „ „ „ A
Neither A nor B serum, „ „ „ O

THE FATE OF TRANSFUSED BLOOD

It is of some importance to know how long the effect of a transfusion can be expected to last for red corpuscles are not immortal Theoretical calculations of this time based on observations on normal individuals must necessarily be unreliable as they take no account of the response of the host to the transfused blood, nor does it follow that conditions will be as favourable for the transfused cells in a diseased subject The information may be of value in two directions, for example in determining how long before an operation to give a transfusion, for instance before splenectomy for thrombocytopenia, or in deciding when next to transfuse an anaemic patient who is receiving repeated transfusions, as the replacement effect of the transfusion can only be expected to last as long as there are red cells in circulation

The life of a red corpuscle has been determined in two ways

By the transfusion of blood of a different group (Ashby, 1919) If for example an individual of group A is transfused with blood of group O, the presence of the transfused cells can be determined indirectly by repeated observations of the blood count The count is made in the usual way except that an anti A serum is used instead of the ordinary diluting fluid The serum agglutinates the A cells leaving the O cells unagglutinated A count is made of the inagglutinable cells these include not only the transfused group O cells but also 50 million per cubic millimetre of inagglutinable cells which it has been shown are normally present As long as the count of inagglutinable cells exceeds the number of those normally present the existence of donor cells in the circulation may be assumed

By this method Ashby has found transfused red cells in the recipient's circulation up to 100 days after transfusion, and Wearn, Warren, and Ames (1922) found an average survival

time of 83 days See also Dekkers (1939), Hawkins and Whipple (1938)

These figures represent maximum survival times The red cells introduced at transfusion are of all ages Some are already dying, others are still immature The effective therapeutic period probably does not exceed fourteen days

By means of the factors M and N With the aid of these factors Landsteiner, Levine and Janes (1928) and Wiener (1935) were able to confirm the findings of Ashby

If a recipient of group A containing the factor N is transfused by a donor of the same group containing the factor M and the blood is re examined from time to time with anti M serum, the presence of donor cells can be assumed, for as long as agglutina tion continues to take place

The life of the white cell

The life of a polymorphonuclear cell is very short—from 3 to 5 days

The survival time has been determined by continuous observa tion of stained specimens over 8 hours (Sabin Cunningham, Doan, Kindwall (1925)) During this period it was found that *6* per cent of the total polymorphs were senile i e *18* per cent in 24 hours or approximately one fifth of the total count were destroyed in one day

The life of the platelets

The duration of life of a platelet is unknown Platelet counts following transfusion to essential thrombocytopenic subjects show that the transfused platelets have disappeared from the circulation in 3 to 5 days but there is evidence to show that in such patients, platelet shortage is due to continuous rapid destruction

SUB-GROUPS

Groups A and AB have been divided by von Dungern and Hirschfeld (1910) *into* sub groups A_1, A_2 *and* A_1B A_2B respec tively This subdivision was discovered by exposing the cells of these groups to the α serum of group B before and after absorption It was found that the majority of α sera have two factors, one of which agglutinates all group A (and AB) cells,

the α factor, and one which agglutinates the majority of A (and AB) cells, the α_1 factor In other words most A cells have two agglutinable bodies, but a minority have only one This divides A cells into two types, the majority—A_1—agglutinated by α factor and by α_1 factor, the minority A_2 agglutinated by α factor only It will be seen that this subdivision of the groups A and AB is based on the agglutinogen factor in the cells and that no mention is made of the development of a corresponding agglutinin It may be wondered what the significance of these sub groups is in the practice of blood grouping, and how it is that incompatibilities are possible between individuals of the same group between whom the only apparent difference is a qualitative one affecting the agglutinogen factor only If, for instance sub group A contained an agglutinin which was antagonistic to the agglutinogen present in sub group A_2 cells, then the incompatibility could be explained Landsteiner and Levine (1929) have shown that such atypical agglutinins are in fact present in approximately 3 per cent of individuals

The presence of these atypical agglutinins and sub groups does not in any way interfere with the scheme of the four blood groups or affect the interpretation of the blood groups as determined by the use of typing sera

Their importance as a cause of transfusion reactions is discussed under that heading

THE AGGLUTINOGENS M AND N OF LANDSTEINER AND LEVINE

In 1927 Landsteiner and Levine revealed the presence in human red blood corpuscles of agglutinable factors unrelated to the agglutinogens A and B These factors were named M and N, and one or other was found always to be present in any given sample of blood The M and N factors are distributed irrespective of group or sub group, and since their corresponding anti M and anti N *isoagglutinins* are not present in the serum these factors do not play any role in the selection of donors for transfusion or in the preparation of sera for stock typing purposes

The practical application of our knowledge of the existence of the factors M and N may be turned to advantage in the following circumstances

1 With the aid of these factors, it has been possible to detect donor blood cells in the circulation of the patient in cases in which compatible blood has been used but the donor, for instance, has been M and the recipient N By examining the blood of such a recipient from time to time it is possible to determine the life of the red blood cell

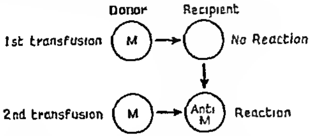

Fig 19

2 A possible part played by the M and N factors in transfusion may be in connexion with certain unexplained *re transfusion reactions* As the result of the formation of anti M or anti N agglutinins induced by a previous transfusion from a donor containing the factor M or N in his cells, an antigen antibody reaction may take place This is discussed further in the chapter dealing with reactions

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CHAPTER VIII

COMPLICATIONS OF BLOOD TRANSFUSION

'Appreciation of the dangers attending the practice of blood transfusion has varied greatly at different times In the seventeenth century a happy ignorance took no account of them whatever In the eighteenth century they were so greatly feared that transfusion fell into abeyance In the nineteenth century it was realized that dangers existed, but they were imperfectly understood, when fatalities occurred, a partial knowledge explained them away more easily than our fuller knowledge can to-day, so that transfusion was practised in spite of them At the beginning of the twentieth century, with the discovery of "blood groups", it was thought that all danger had been eliminated At the present time the pendulum is swinging back again, and the problem of the complete elimination of danger is proving more complex than it was thought to be a few years ago' (Keynes, 1922)

CIRCULATORY FAILURE AND PULMONARY OEDEMA

Circulatory failure is the commonest cause of a fatality following blood transfusion. It may be due directly to *overloading* of the circulation or it may develop secondary to a *rigor*

From primary overloading.

A case of pulmonary oedema following *direct overloading* of the circulation is described by Plummer (1930)

The case was one of obscure anaemia in a woman aged 26 with mitral stenosis The blood group of both patient and donor was Moss II The direct test showed no incompatibility The haemoglobin was 35 per cent, red cells 2,480,000 She was given 600 c c of citrated blood

'During the transfusion the patient developed a *mild dry cough*, and *immediately afterwards she felt sick Forty five minutes later she* collapsed and was grey in colour Adrenaline 5 m and, an hour later, morphine one quarter of a grain with atropine one fiftieth grain were given because of pulmonary oedema, but the patient died 2 hours after completion of the transfusion At autopsy the heart showed dilatation and hypertrophy of both auricles and the right ventricle, and the lungs were bulky, deeply engorged and oedematous'

Fig. 20. A dilated heart in a case of long standing secondary anaemia. Blood transfusion to such a patient can only be given with safety at a *drip rate*.

In an individual whose blood volume is normal, that is to say not depleted by haemorrhage, the production or not of circulatory failure following the intravenous infusion of fluid depends on three main factors: the volume of blood introduced, the rate of its introduction, and the mechanical efficiency of the cardiac muscle at the time.

A large volume of blood introduced slowly may give rise to no symptoms, whereas a small volume introduced rapidly may produce heart failure. If at the time of the transfusion the patient is gravely ill and particularly if he has an *anaemia of long standing*, the mechanical efficiency of the heart will be

proportionately reduced, and indeed it may already have begun to fail In such circumstances a transfusion of normal volume and given at normal speed may so increase the venous return that the balance between income and output, which before the transfusion was just maintained, is disturbed, and the anaemic or toxic myocardium fails

Secondary to a rigor.

A case of pulmonary oedema developing *after a rigor* is described by Pygott (1937)

'The case was one of pernicious anaemia with subacute combined de generation of the spinal cord in a man aged 50 The blood group of both patient and donor was Moss IV The direct test showed no incompatibility The haemoglobin was 25 per cent He was given 550 c c of citrated blood

'There was no immediate reaction of any kind, but one hour later the patient complained of feeling cold and had a *rigor* He was given hot drinks, and he settled down again with no further complaints until four hours after the transfusion, when he suddenly collapsed and went into a coma, with cyanosis, dyspnoea, and a feeble pulse His chest was then full of bubbling rales, and he died an hour later At necropsy the lungs were found to be oedematous, the heart was slightly dilated and its muscle was very flabby and showed a typical thrush breast appearance '

It is pointed out on p 73 that the danger of the ordinary febrile reaction is the rigor which may accompany it A myocardium with sufficient reserve strength to deal with a relatively rapid increase in blood volume may find itself quite unable to maintain the circulation of the blood in the event of such a constitutional disturbance as a rigor Plummer (1936) reported four deaths due to circulatory failure One of these was an example of straightforward overloading of the circulation in a patient with mitral stenosis, described above but the other three cases only developed signs of heart failure following a rigor All these patients had been anaemic for a long time, in other words the heart-muscle was not normal Acute pulmonary oedema was the most striking feature at necropsy in these cases Two other examples of circulatory failure with pulmonary oedema are reported by DeGowin (1938), in which there was no reaction of any kind to the introduction of blood, but which collapsed and died following a rigor

I believe that death in these circumstances is very much commoner than is generally supposed and that the connexion

between cause and effect is not always appreciated, particularly if death is delayed for several hours after the transfusion

TREATMENT OF CIRCULATORY FAILURE

Prophylaxis

The selection of cases for intravenous therapy.

The prevention of these catastrophes lies in acquiring a proper regard for intravenous therapy of all kinds, and for all types of patients To this end the patient's cardiac reserve must first be determined before it is decided actively to increase the volume of circulating fluid by transfusion

Secondly every precaution must be taken to avoid a rigor, particularly in the anaemic This can only be achieved by attention to those details affecting the apparatus the operator, and the patient which are stressed on p 78

Additional precautionary measures which may be taken include

Preliminary venesection From time to time it happens that a case unsuitable for intravenous therapy must be transfused to save life In these circumstances—assuming the transfusion is not to replace blood lost—a venesection should precede the actual introduction of the blood On a number of occasions I have found this a most satisfactory solution to the problem The amount withdrawn will depend on the volume which is to be transfused and the rate at which it is intended to introduce the new blood

Drip transfusion It is now a matter of common experience that overloading of the circulation and severe reactions occur less frequently if the blood is introduced by a drip method For this reason *all gravely anaemic individuals should be transfused at a drip rate* To give a short quick transfusion in these cases is to court disaster

Transfusion of cells or serum only To reduce the bulk of fluid introduced a transfusion of red cells only or of the separated plasma may be used The serum forms more than half by volume of any given sample of blood so that on occasion when the formed elements are not required it may be convenient to transfuse the citrated plasma only

During Transfusion

The symptoms of cardiac embarrassment

Early recognition of the symptoms of cardiac embarrassment —that is while the transfusion is still in progress—may avert disaster The first and most constant symptom is a *dry cough*

Pygott says that it is possible to produce in almost any patient a fit of severe coughing in the course of a transfusion by accelerating the rate of introduction after about 150 c c have been given He thinks that this may be ascribed to a temporary over distension of the right auricle, which may also account for the *constricting sense of pain* felt in the chest on these occasions (Pygott, 1937)

In the event of pulmonary oedema developing

If circulatory failure develops in the course of a transfusion an immediate venesection should be performed The introduction of adrenaline at this stage is absolutely contra indicated as it can only further embarrass the heart's action Atropine grain one fiftieth should be injected subcutaneously to arrest bronchial secretion together with morphine grain one quarter, to relieve the heart In some cases even aspiration of the bronchial tree may be needed

THE COMMON FEBRILE REACTION

By the common febrile reaction is meant the most usual reaction following a transfusion of blood involving in its simplest form no discomfort to the patient but a rise of temperature to 100° F In its severest form there is a rigor followed by a rise of temperature to the region of 104° F

The *danger* of this type of reaction is in the extra strain thrown upon a myocardium frequently much weakened by long standing anaemia Such a rigor, though it may not directly harm the patient, may, as the result of the increased burden put upon the heart, bring about a mechanical failure with pulmonary oedema from which the patient may die This point is emphasized so that the real danger of rigors may be appreciated and every care taken to avoid them

In addition, a rigor is an alarming experience and should the

patient require a subsequent transfusion it is likely to be very difficult to get him to submit readily

Pulmonary oedema following a rigor

An example of a case of pulmonary oedema developing after a rigor is reported by Plummer (1936) (See also Pygott, p 71)

Details

A case of Addison s anaemia in a woman aged 60 The blood group of both patient and donor was Moss II and the direct test showed no incompatibility The haemoglobin was 30 per cent She was given 300 c c of citrated blood

Shortly after completion of the operation she experienced a sense of fulness in the throat and *shivered* slightly An hour and a half after commencement of the transfusion the pulse rose to 140 and the temperature to 100° F pulmonary oedema developed The patient became comatose and died 10 hours after the transfusion At necropsy the bases of the lungs were congested and oedematous The heart muscle was soft and the right side was dilated

The belief that those who have a rigor respond better to the transfusion is only rarely confirmed in practice and does not justify us allowing post transfusional rigors to go uninvestigated

Behaviour of haemoglobin in the recipient after transfusion In a series of 77 non bleeding cases which were transfused at the Mayo Clinic (Sibley and Lundy 1938) it was observed that in those cases in which there was no reaction the rise of haemoglobin in the recipient was almost twice that of those cases which had a reaction This rise of haemoglobin was not maximal until approximately 48 hours after the transfusion

The cause of the common febrile reaction

In the majority of cases these reactions are believed to be due to the *injection of foreign protein* in some form and this is supported by

(i) The similarity of the picture to that of serum shock
(ii) The exclusion of the citrate factor by Lewisohn and Rosenthal (1933) (p 184)
(iii) The fact that reactions are commoner in recipients sensitized by previous transfusions or possessing an allergic taint

The injected foreign protein may take the form of old blood clot left in the apparatus or may be the result of air borne contamination of the blood or solutions by bacteria (p 184)

In a smaller proportion of cases the febrile reaction is due to *technical faults* in the conduct of the transfusion Such faults will include errors in collecting the blood so that the flow is intermittent, inadequate citration of the blood which may allow minute coagulative changes to take place and inaccurate temperature control which may allow cold agglutinins to become effective Failed intravenous puncture or venesection by distressing the patient and by prolonged exposure also dispose towards a reaction

The importance of a sound technique was shown very convincingly at the Mount Sinai Hospital in New York when the conduction of transfusions was taken out of the hands of recently qualified students and its practice limited to senior residents or members of the staff In the course of a year (1922) there was a reduction in the reactions from 23 to 13 per cent Similar observations in this country have borne out the importance of a proper experience in producing the best results

In London the Red Cross Blood Transfusion Service insists that only senior residents may withdraw the blood from their donors Such a rule is in the interests of both donor and recipient as technical hitches at this stage may influence both unfavourably

In a few cases a febrile reaction is probably due to *minor incompatibilities* such as may occur with a high titre donor or in the rare event of the presence of accessory agglutinins Incompatibility between the white cells has been suggested by Doan (1926) in instances where all the more probable factors have been excluded

Frequency of reactions

The frequency of febrile reactions varies considerably from author to author Certain transfusers declare that they 'have never seen a reaction'. This is generally because they do not visit the patient again after the transfusion and because in the interpretation of these observers anything short of a genuine rigor is not regarded as a reaction For statistical purposes it is convenient to recognize three grades of febrile reaction

Grade i associated with a rise of temperature to 100° F but no other objective features

Grade ii associated with a similar or greater rise of temperature and subjectively with feeling cold and shivery but without having an actual rigor

Grade iii associated with a definite rigor the so called post transfusion chill of some writers

It is very easy to deceive oneself about the frequency of reactions My *impression* was that in my own hands they had fallen to below the 5 per cent mark (1938) But on analysis I found that 11 out of the last 100 cases I transfused had rigors These transfusions were all personally conducted and observed throughout

The reaction rate is enormously influenced by the *indication* for the transfusion and by the *rate* of introduction of the blood Haemorrhage cases rarely rigor the chronic anaemias and in particular septic cases have a high reaction rate in my experience

Reaction statistics are therefore of little value unless they are considered in relation to the indications and rate of introduction of the blood

Kordenat and Smithies (1925) state that practically all transfusions if carefully watched are followed by some rise of temperature though this is likely to be symptomless My own observations are in agreement with this statement

Lewisohn and Rosenthal (1933) using the citrate method report only 1 2 per cent of rigors This compares on level terms with any whole blood method but a careful preparation of apparatus is essential to keep to this low figure below which neither advocates of whole blood nor citrated blood have so far been able to reach however careful they may have been

The Treatment of a Febrile Reaction

Arising during transfusion

If the patient feels shivery while the blood is being injected and a rigor seems imminent the transfusion should be stopped and the needle withdrawn

The subsequent treatment is outlined below (collapse should be treated along general lines with warmth and stimulation)

Arising after transfusion.

Feeling cold. Immediately the patient complains of feeling cold or chilly, a *hot water bottle* should be placed in the bed, and he should be wrapped up and made as warm as possible

Shivering If the feeling of coldness develops into actual shivering, a *subcutaneous injection of adrenaline (6 minims of* a 1/1,000 solution) should be given The adrenaline is given in case the reaction has an anaphylactic or allergic basis and *not* as a cardiac stimulant It should not be repeated if it is ineffective at the first injection, as more of this drug will only serve to embarrass the heart

If the patient is having a *severe rigor* which has not been relieved by adrenaline, an injection of *morphine* one quarter grain should be given immediately Morphine tends to shorten the attack, it relieves the right heart and it quietens an anxious patient by providing the sleep which is so badly needed after the physical exhaustion and mental distress produced by such a reaction

It is my own practice to give an injection of *atropine,* one fiftieth grain, at the same time as the morphine Atropine, if administered early and adequately in this way and particularly if combined with morphine, tends to prevent the excessive pulmonary and bronchial secretions which may so quickly collect and drown the patient

In a small volume transfusion taking 45 minutes to give, a rigor, if it is going to occur, will usually begin within a quarter of an hour of the end of the transfusion i e within an hour of the start It is generally safe to tell the nurse or relations that there will be no rigor if it has not occurred within this time *The slower the transfusion, the less likely is a rigor to follow*

Collapse. Collapse should be treated along general lines with warmth and stimulation

Subsequent procedure.

(i) A note of a severe reaction should be made and the service supplying the donor informed so that a careful check

may be kept upon him. Certain donors seem to cause more reactions than others, sometimes because they are high titre group O s being used as universal donors, sometimes because they are group A s or AB s with sub groups.

(ii) An investigation into the cause of the reaction should be carried out along the lines suggested at the end of this chapter.

Prevention of reactions

The occurrence of the febrile type of reaction can be reduced to a minimum by

Preparation Careful preparation, cleansing and sterilization of apparatus and solutions.

Speed Introducing the blood at a drip rate—40 drops a minute.

Technique Employing a simple and reliable technique which avoids cutting down and avoids prolonged exposure of the patient.

Temperature Accurate temperature control in the more rapid type of transfusion.

Patient Keeping the patient warm during and after the transfusion.

General management Conducting the transfusion with the care accorded to more extensive operations, in other words avoiding talking and noise which may exhaust the patient. To this end the room should be darkened after the transfusion is over and the patient induced to go to sleep with the help of drugs if necessary. It is often good practice to give omnopon, one sixth grain at the end of the transfusion.

Retransfusion following a rigor

If a patient who has had a rigor at a previous transfusion is to be *retransfused* it will be wise to take certain precautions.

1 The most important single measure is to introduce the blood at a slow drip rate—in an adult 40 drops a minute.

2 Additional precautions are

(i) The same donor should not be used again.

(ii) The direct compatibility test should on no account be omitted.

(iii) If the patient is group A it will be worth while trying him with group O blood

A patient of group A with aplastic anaemia, to whom I gave 27 transfusions, could only tolerate blood from group O donors Whenever we returned to a group A donor there was a severe reaction with a rigor

(iv) Rarely a whole blood transfusion may suit the patient better.

AIR EMBOLISM

The dangers of embolism following the entry of air into the veins of the elbow region appear to have been generally exaggerated. My own experience is that bubbles of air have frequently been introduced and no ill effects have been noticed

If a large volume of air is injected or aspirated it may produce heart failure, either directly by over distension of the right auricle, or, in the rare event of a patent inter auricular septum, by distension of the left auricle

Shulman and Glass (1937) were only able to find one fatal case of air embolism following intravenous injection at the elbow, in the literature of the period 1928–37 These observers have on two occasions introduced 30 c c of air during transfusion in man without noticing any ill effect Nordland (1930) and his co workers have had similar experiences

In the course of a transfusion, then, the entrance of a few bubbles of air need not be a cause of alarm, although they can hardly be regarded as evidence of a good technique

AGGLUTINATION IN THE COLD

Stewart and Harvey (1931) have reported two interesting cases in which cold agglutination was observed in the cross matching test, but transfusion was carried out in spite of this Both patients were severely anaemic, both had severe reactions of a febrile type without haemolysis, and both cases recovered In each instance the donor was of group O and the recipient of a different group

In practice one should anticipate a probable reaction when cold agglutinins are known to be present A reaction is *prevented by*

1 Maintaining the temperature of the blood at 37° C throughout the transfusion.

2 Introducing the blood at a drip rate
3 Keeping the patient warm during and after the transfusion
4 Injecting morphine and adrenaline if there is any sign of collapse

There is a further discussion on cold agglutinins on p 35

ANAPHYLAXIS AND ALLERGY

Anaphylactic and Allied Reactions

Anaphylactic shock

Occurrence of severe anaphylactic shock following blood transfusion must be excessively rare and it is significant that no case has been reported to the Medical Officer of the London Blood Transfusion Service in the last seven years during approximately 30 000 transfusions

True anaphylaxis presumably could occur in a second or subsequent transfusion if the recipient had been sensitized by some foreign protein in a previous donor s serum possibly food circulating in his serum But the repetition of such a factor is extremely improbable

These cases are always difficult to prove but it seems likely that these circumstances were present in a case reported by Duke and Stofer (1924) in which the recipient was sensitive to cow s milk and at his second transfusion developed symptoms suggestive of anaphylactic shock after receiving blood from a donor who had recently had cow s milk to drink In this case no mention is made of the first donor having taken cow s milk the circulating proteins of which would have acted on the necessary antigen but it is probable that this is what happened In some cases a meal of eggs appears to have provided the offending protein

Although from a clinical point of view true anaphylaxis and the similar type of reaction which follows blood transfusion would appear to be the same from a biological and immunological standpoint the two reactions would appear to be wholly dissimilar

The fact remains however that a considerable proportion of the reactions following blood transfusion have produced in

varying degrees of intensity, a clinical condition exactly resembling the well known picture of anaphylactic shock which follows the injection of horse serum to an individual who has been sensitized by a previous dose In most of the cases following blood transfusion however no such previous sensitization can be traced

A case of death following this type of reaction in which there was no history of asthma hay fever, or other signs of protein sensitization in either donor or recipient, has been reported by Carrington and Lee (1923)

The patient had pernicious anaemia After very careful matching (with a number of donors) the patient was transfused by the citrate method with 500 c c of blood without any immediate reaction One half hour afterwards however he developed a typical anaphylactic protein reaction with high fever spasm of the unstriated muscles asthmatic symptoms in the lungs involuntary voiding the urine and several bowel movements This subsided after one hour but the man developed acute oedema of the lungs and died eight hours after transfusion During the reaction the urine was examined and no haemoglobin found The blood showed no haemolysis or agglutination

Anaphylactic and similar reactions can be distinguished from haemolytic shock because in anaphylaxis (1) the onset of symptoms is earlier, if not instantaneous and can be produced by a minute dose of the antigen (2) there is no evidence of haemolysis viz jaundice haemoglobinuria haemoglobinaemia or positive Van den Bergh and (3) there are no kidney symptoms

As will be seen in the next paragraph it has recently been suggested that some at least of the so called 'anaphylactic' reactions are manifestations of speed shock that is to say reactions on the part of the body to the too rapid introduction of blood

Speed shock

Hirshfeld, Hyman, and Wanger (1931) have suggested an alternative theory to explain the cause of the anaphylactic type of reaction following blood transfusion, based on experimental work These authors state that in dogs and rabbits an exactly similar clinical syndrome can be reproduced *by rapid intravenous injections* of fluid In short, they believe that the

common anaphylactoid phenomenon is a velocity reaction and they refer to it as *speed shock*

Their claim is supported experimentally by the various phenomena accompanying the rapid injection of fluid into animals They observed that the speed shock reaction began within 40–60 seconds of the commencement of the injection that it was associated with cardiac failure shown graphically by a deep fall in blood pressure that it was accompanied by evidence of respiratory distress sometimes in the form of dyspnoea and spasm of the bronchial muscles sometimes as apnoea with muscular atony

It is their belief that the site of action of speed shock is in the liver cell since the clinical condition cannot be produced in hepatectomized animals They suggest that as a result of temporary cell damage some potent substance is liberated by the liver cell and that the syndrome described results in the circulation of this substance The fact that production of a shock picture occurred with a variable list of chemical substances supports the contention that it is due to some constantly present factor for example the velocity of introduction of the blood

So far as I know this work has not yet been confirmed on human beings nor has the toxic substance of alleged hepatic origin been isolated but even as unsubstantiated experimental investigations they are of the greatest interest and drive a formidable wedge into the loose and vague phraseology of the anaphylactic nomenclature

Allergic Reactions and Urticaria

In practice as well as for descriptive purposes the use of the term allergic type of reaction is best confined to those instances only where evidence of natural hypersensitivity can be obtained either in the donor or the recipient Such a reaction may occur at a first transfusion or not until later

If the donor has any allergic taint for example hay fever and is in the active phase at the time of the transfusion he may transmit this tendency to a recipient

In the same way if the recipient is sensitive to any substance circulating in the donor s serum a similar reaction may occur

Clinically these reactions are usually mild and unassociated with any marked constitutional symptoms, and are as a rule accompanied by a varying degree of urticaria and eosinophilia

Examples of this type of reaction have been reported by numerous observers

Sensitive recipient.

Goodall (1938) reports the case of a woman who was receiving a trans fusion when she suddenly developed urticarial symptoms The trans fusion was stopped and after injection of adrenaline, was resumed When questioned upon her reactions to food the patient stated that the only ingredient she knew she could not take was gin It always produced urticaria and she had not touched it for 15 years When the donor was asked how much gin he had had that morning he confessed (in some alarm) to having had one drink

A similar case in which the recipient was sensitive to cockles and where the donor had had a meal of cockles previous to the transfusion is reported by Stewart and Bates (1938)

Sensitive donor.

(a) In the active phase at the time of the transfusion. Tedstrom (1933) reports the case of a donor who had urticaria, at the time that his blood was withdrawn, from eating straw-berries the recipient developed urticaria immediately following the transfusion

(b) In the inactive phase. This amounts to the transmission of hypersensitivity The classical example was reported by Ramirez (1919) who observed that a donor sensitive to horse dandruff—he used to get asthma—transmitted this tendency to a recipient who, although not sensitive before the transfusion, afterwards used to get asthma when she went near a horse

A similar type of case of the transmission of hypersensitivity is reported by Holder and Diefenbach (1932) In their case the donor was sensitive to strawberries After the transfusion the recipient became sensitive as shown by urticarial rashes on eating strawberries This transmitted sensitivity passed off in a year

No history of hypersensitivity.

These are the commonest cases of all and are most likely to occur in patients receiving multiple transfusions Thurston

(1938) reports such a case and I have had experience of three—each in transfusions after the first and each showing urticaria of varying intensity and distribution

A fatal case in the allergic category is reported by Hancock (1936) In this case death occurred 10 hours after the transfusion and the clinical picture preceding death was suggestive of a cerebral oedema analogous to the urticaria of the skin which was also present There was no evidence of haemolysis or agglutination

Until we know more of the subject we can unfortunately do no better than put down many of the unexplained reactions producing this type of clinical picture to some allergic taint in the recipient or donor although in many cases a hypersensitive factor cannot be elucidated in the history of either

Treatment

In any transfusion to an allergic patient but particularly after the first it will be wise to use a fasting donor

In anticipation of a reaction of this type it is a good practice to give ephedrine half a grain in tablet form by the mouth half an hour before the transfusion

If the *patient* is known to be allergic it will be advisable to give him a small intradermal injection of the donor s serum as a sensitivity test This will take only a few moments and may give valuable information

If the *donor* is allergic he is relatively safe to use except during the active phase of his condition Such donors should be advised to sign off from service for three months during the summer if they suffer from hay fever Others should be advised not to serve during an active phase

Reactions of the allergic type respond well to the hypodermic injection of adrenaline An initial dose of 7 minims of 1/1 000 adrenaline hydrochloride should be given and then 1 minim per minute until the effect is obtained

HAEMOLYTIC REACTIONS IN SPITE OF CORRECT GROUPING

Haemolytic reactions occur not only when the blood introduced is of an incorrect group but also when donor and recipient are of the same blood group Such haemolytic reac

tions are usually less severe than when a donor of a wrong group is used The main clinical features are the same, only they are less marked

Theoretically, the conditions under which haemolysis may take place apart from the main one of wrong grouping are

Intravascular Haemolysis i e haemolysis in vivo

1 On retransfusion
2 When using a group O as a Universal donor (p 50)
3 *In transfusing the haemolytic anaemias (p 153)*
4 By interaction of sub groups

Haemolysis outside the body, i e haemolysis in vitro

1 Overheating the blood (p 250)
2 Freezing the blood (p 307)
3 Overstorage (p 306)
4 Reinfusion of blood more than 72 hours old from body cavities (p 294)
5 Mixing the blood of two or more donors (p 256 (IV))
6 Shaking the blood (p 309)

Retransfusion Reactions

Melnick and Cowgill (1937) of Yale University working on dogs found that retransfusion shock occurred in dogs retransfused *after more than one week s interval*—both from the same and different donors The period of sensitivity or haemolytic interval following the first transfusion lasted up to 10 weeks, during which time the serum of the recipient would haemolyse the cells of the donor To what extent such a period of sensitivity exists in man is not yet known but there is no doubt that a patient receiving multiple transfusions is more prone to a haemolytic reaction than a patient receiving his first transfusion A 'safe period' has not so far been worked out in man By analogy with Melnick and Cowgill s work on animals it seems probable that the earlier retransfusion is carried out the less likely is a haemolytic reaction to follow Retransfusion after an interval of more than a week should always be accompanied by careful cross matching

A Same donor twice

Occasionally it happens that the use of the same donor on more than one occasion for the same recipient is followed by a

severe haemolytic type of reaction. Traum (1932) reports a case in which there was a severe haemolytic reaction 18 months after the previous transfusion from the same donor. Other cases have been reported by Plummer (1936), Thalhimer (1921), Levine and Segal (1922), Astrowe (1922), Smith and Haman (1934), Duke and Stofer (1924), but there is little doubt that there are many transfusions in which the same donor is used on successive occasions which are unassociated with any form of reaction. Characteristically there is no reaction at the time of the first transfusion—it is at the second or third transfusion that the reaction occurs.

The reaction can be explained by assuming the presence of an additional agglutinogen (C) agglutinin (γ) pair of factors. The production of an antibody in response to stimulation by an antigen is a well known immunological phenomenon. The production of such an antibody (agglutinin) following a transfusion may be represented thus:

	Donor		*Recipient*	
1st transfusion	$C\alpha\beta$ (apparently group O)	$\longrightarrow$	$\alpha\beta$	No reaction
2nd	$C\alpha\beta$ ( )	$\longrightarrow$	$C\alpha\beta\gamma$	Reaction $(C \times \gamma)$

At the first transfusion the agglutinogen C was introduced. The recipient responded by forming the agglutinin (γ). This (γ) reacted with the original agglutinogen C when this C was reintroduced at the second transfusion.

Treatment. The "same donor twice" type of reaction can be avoided by conscientious repetition of the cross matching test before the second transfusion. *Provided the direct test is satisfactory* the same donor may be used again and again with perfect safety.

The developed reaction will be treated in the same way as other haemolytic reactions, the exact treatment depending on the severity of the condition.

B. Reactions possibly due to the factors M and N

Reactions following the use of different donors for the same patient are reported from time to time. In some instances the donors used on successive occasions have been of different

groups As these reactions are usually haemolytic in type, that is to say involving the destruction of red corpuscles, they cannot be explained as being due simply to interaction between substances in the sera of the two individuals concerned

The reaction appears to be due to the development of agglutinins in the serum of the recipient against an antigen present in the red corpuscles of the donor introduced in the previous transfusion As the reaction can take place even when donors of different groups are used, it is necessary to postulate an agglutinable substance which is distributed in the corpuscles, irrespective of group Two such antigenic substances have in fact been found in the agglutinogen factors M and N, and it seems probable that the introduction of blood containing one of these factors will result in the formation of the corresponding anti M or anti N agglutinin in the recipient's serum In these circumstances, when a second transfusion is made of corpuscles containing the factor M or N a reaction may occur

Since the agglutinogens M and N may also be distributed in the cells of members of group O, these factors may account for some of the hitherto unexplained reactions following the use of the universal donor on more than one occasion to another member of this group (Fig 19)

Treatment. The danger of such reactions may be obviated by the preliminary direct compatibility test Compatibility determined by grouping alone will not reveal such an anti agglutinin

C. Unknown factors.

As the result of a previous transfusion either from the same or different donors, the opportunity for irregular immunological reactions must be correspondingly increased and haemolysins may develop which may cause haemolysis of any donor's cells The point to bear in mind is that such an acquired haemolysin will be detectable if the ordinary cross matching test is carried out, since for each haemolysin formed there is at the same time an agglutinin produced, and agglutination precedes haemolysis in the cross test, this being the order of events upon which reliability of the test is based

In rare cases agglutination apparently does not precede

haemolysis that is does not occur at all presumably due to the failure of the corresponding agglutinin to develop. From a practical point of view the rare case in which a haemolysin develops without a corresponding agglutinin, and so is not detected in the cross matching should be disregarded. They must be excessively rare, perhaps once in 20 000 transfusions, and should not be allowed to influence our confidence in the cross test.

The only way to detect such a haemolysin will be to test separately for it. Since haemolysin only acts satisfactorily at a temperature of 37° C and in the presence of complement, it will be necessary to obtain guinea pig's serum or human serum of the same group to supply complement and heat together in a water bath for at least 2 hours. Such an interval removes the test for haemolysins from the sphere of practical medicine, except when there is no urgency attached to the case. I think that the proper attitude to adopt towards this rare event is that of bearing it in mind when searching for the cause of an unexplained haemolytic reaction.

Sub-group Reactions due to the Presence of Accessory Agglutinins (Anomalous, Atypical, Adventitious, Intra-group Agglutinins)

In any given case of an unexplained haemolytic reaction the chances are that the fault will be found to lie in the *initial group* determination. Only after wrong grouping has been very carefully excluded by retyping both donor and recipient with high titre sera should adventitious agglutinins be regarded as the cause of the reaction.

Reactions due to the presence of accessory agglutinins are probably very rare, and for these reasons: Landsteiner and Levine (1928) only found an accessory agglutinin present in 3 per cent of individuals; when present the agglutinins were almost invariably of low titre and, furthermore, were usually inactive at body temperature. The distribution of the atypical agglutinins was found to be as follows:

1. Found in individuals of sub-group A_1 and A_1B and acting only on bloods of groups O and sub-group A_2.

2 Found in individuals of sub groups A_1 and A_2B and acting only on bloods of sub group A_1
3 Acting irrespective of group

This distribution of accessory agglutinins may account for some of the unexplained reactions when a group O has been used as a donor to groups A (or AB) or when a group A (or AB) has been used for another group A (or AB)

A severe haemolytic reaction due to an accessory agglutinin in the recipient s serum is reported by Culbertson and Ratcliffe (1936) whose findings were confirmed by Landsteiner They found that it was necessary to use the centrifuge test method described by Wiener and Vaisberg (1931) to demonstrate the presence of the agglutinins Similar reactions in which the presence of irregular agglutinins has been sus pected though not necessarily confirmed have been reported by McCandless (1935) and Stetson (1933)

Prophylaxis

These incompatibilities will remain unexposed if reliance is placed on the indirect grouping test alone but will be revealed by the direct compatibility test another example of the value of this procedure as a routine measure

The Transmission of Syphilis

Although the transmission of syphilis by transfusion can hardly be regarded as a commonplace—nevertheless it seems probable that it is by no means a rarity

Rein (1938) of New York says that 68 cases have been re corded in the literature and he believes that this is a mere fraction of the actual number of instances occurring (See Bibliography)

The practical points of interest in connexion with this com plication of blood transfusion are related to the prevention of transmission and the time and nature of onset of the first symptoms in the recipient

The prevention of transfusion syphilis

Almost all the recorded cases of transmission have occurred when using paid donors or untested relatives or friends This is one of the strongest criticisms we have had to make of the pro fessional system—namely, that a less reliable member of the

community is attracted to service when there is a prospect of gain

In some countries using professional donors the doctors are advised to make a physical examination of the donor before transfusion for evidence of a primary lesion as such a donor in spite of a Wassermann reaction might still be in the sero negative phase In a long experience these precautions have been found unnecessary when dealing with the members of a voluntary service

There remain however, the untested donors who may have to be used in an emergency and who are probably the most potent source of transmitted disease under either system The tendency in an emergency—and not an unnatural one—is to take a chance with a donor particularly if he is a relative In the urgency of the moment one is often considerably relieved to find a donor of a compatible group without taking further steps to establish suitability in other directions It has been suggested that the reason for this attitude of mind is to be found in the time taken to carry out such tests as the Wassermann reaction For this reason American writers in particular have strongly recommended the use of the Khno flocculation test which can be completed in 20 minutes and the Laughlen (1935) test which takes even less time

When an expert serologist is available it seems likely that these tests have much to be said for them but unfortunately the circumstances associated with an emergency transfusion are rarely so obliging In most instances it will still be more practical to rely on the word of the donor combined if in doubt with a physical examination Fortunately the chances of transmitting syphilis are most marked when some clinical evidence of it is still likely to be found i e in the primary and secondary stages and least probable in the tertiary stage—although of course a donor in the latter stage is by no means to be regarded as non infectious (McNamara 1925)

The onset of symptoms in the recipient

In the majority of patients reported as developing transfusion syphilis the time of onset of the first symptom was 2–2½ months after the transfusion The symptoms were generalized,

most commonly starting with a rash and then pursuing the usual course associated with the secondary stage of syphilis

The Transmission of Malaria

A large number of instances (see Bibliography) of the accidental transmission of malaria by blood transfusion have been recorded

On reading the accounts of these cases the outstanding fact that emerges is that in all but a few the donor was unaware that he had ever suffered from the disease Herein lies the danger of accepting a denial of past infection from any one who has ever lived in a malarial district The explanation is that a latent infection may persist for years without giving rise to symptoms In Nobecourt's (1932) case a donor who did not know that he had malaria, and who had left the endemic area infected a recipient years later, and McCulloch (1937) reports a case of transmission of quartan malaria from father to daughter by blood transfusion in Canada where the quartan type of malaria is almost unknown The father had left Rumania 25 years before and did not know that he had ever had malaria

Dyke (1936) points out that there is another difficulty in identifying the latent malaria carrier, which is that the malarial parasite is rarely present in sufficient numbers in the donor's blood to be demonstrable in ordinary films

Prevention.

In view of the difficulties in identifying latent malarial infection in a prospective donor—partly because a negative history cannot be relied upon and partly because the blood films rarely show the parasite—the only safe method of exclusion lies in regarding all individuals who have resided in a malarial district as potential carriers of the parasite and so unsafe for transfusion purposes

In malarial districts

In actual malarial districts, presumably all donors are suspect In an emergency there will be no alternative but to take the risk of transmitting infection Fortunately the attacks are readily controlled if quinine is administered prophylactically

The Transmission of Influenza

An interesting example of the transmission of influenza is recorded by Levick (1931)

The donor and recipient both belonged to the same blood group (A) The patient was a man aged 36 with pernicious anaemia who was given 520 c c of blood without any reaction on the day of the transfusion Forty eight hours later he developed a typical influenzal attack with shivering joint pains and tenderness over the musculo tendinous junctions which slowly subsided in about 10 days

Some weeks after the transfusion the possibility of infection from the donor was considered and on communicating with him it was found that he had had influenza and was still too ill to leave his house It appeared that he had not been feeling well on the day of the transfusion and on the following evening had been completely overcome with a severe attack of influenza

THE WRONG GROUP TRANSFUSION

Clinical Features

The reaction of a patient to the injection of blood of a different group runs a characteristic course and falls into three well defined phases immediate interval and delayed

In most of the descriptions of wrong group transfusions the reader is rather led to believe that the reaction following may be either immediate or delayed but not both Most commonly however the two are associated being separated by a variable but clearly defined interval attention to which is drawn on this account

Thus the phases are

- **Immediate** reaction due to the sudden acute haemolysis of the incoming donor s cells which is almost invariably followed by a *rigor*
- **Latent interval** of symptomatic improvement but continued oliguria
- **Delayed** reaction characterized by renal failure and uraemia which is followed either by coma and death or diuresis and recovery

These may be regarded as phases in clinical and pathological

progression, the intensity of each being directly proportional to the sensitivity of the patient and the amount of blood introduced

PHASE 1 THE IMMEDIATE REACTION

The immediate reaction occurs during the actual injection of the blood, sometimes after not more than 10 c c have been introduced This very early onset of warning symptoms forms the basis of the 'biological test' so widely used by the advocates of whole blood

Subjectively

It is ushered in by classical subjective symptoms which are in their usual order of appearance a bursting feeling in the head, generalized tingling sensations and later severe lumbar backache **Lumbar backache** is pathognomonic of the transfusion of incompatible blood and is a danger signal that must not be ignored On its appearance the transfusion should immediately be stopped however well the patient may otherwise appear to be In addition, there is commonly a praecordial oppression and dyspnoea and the patient tends to be mentally anxious and restless The throbbing in the head later gives way to severe headache These symptoms are rapidly followed by *collapse*, which may be very severe The phase culminates with a sharp post transfusional *rigor*

Objectively there is flushing of the face, which later becomes cyanotic, and the veins of the neck are distended At this time there may be nausea and vomiting and sometimes urticaria which may be limited to the face or generalized over the body The pulse characteristically drops about twenty beats a minute to start with, but later becomes thin and rapid as the patient becomes cold and clammy and the collapse becomes more marked (Pemberton, Keynes, 1919)

Rarely there is *no immediate reaction*, the first untoward sign being the rigor at the end of the first phase In such cases the prognosis is not so good since the whole quantity of blood is likely to have been given If the injection is stopped with the first appearance of alarming symptoms and so only a small amount injected, the interval phase may pass off with

haemoglobinuria only and the terminal phase never develop at all. Only very rarely does death occur during the immediate haemolytic reaction, and so far in the literature I have been unable to find a single case of death occurring during the immediate reaction of a wrong group transfusion. There were no instances in Bordley's series of cases, and I have been unable to trace any in the British literature. A number of cases of severe haemolytic reaction and one death (Parr and Krischner, 1932) have been reported in apparently correct group transfusions.

Phase 2. The Interval Phase of Symptomatic Improvement

The interval phase, lasting on an average 4 days (2–7 days), is associated with a period *of apparent clinical improvement*, but is marked by haemoglobinuria in the first specimens, and oliguria or anuria subsequently. Jaundice, if it is going to develop at all, and it does not necessarily do so, appears during this stage about 24 hours after the transfusion has been given, and disappears before the delayed reaction sets in. The depth of jaundice is not related to the amount of blood transfused. During this period the patient usually eats, drinks and sleeps well.

Phase 3. The Renal Phase

The term delayed reaction is an unfortunate one, since it implies that the onset of symptoms attributable to the transfusion is delayed unusually long. Such is not the case, since all "delayed reactions" have passed through the preliminary initial stages already mentioned, which are just as characteristic as the terminal but longest phase. It is true that in rare instances there has been no immediate reaction, the first untoward symptom being the immediate post-transfusional rigor, but this is atypical.

Following an uncertain interval period the onset of symptoms *of uraemia is usually quite sudden. All the features of renal* failure are now present, with retained nitrogenous products and the blood urea rising daily, so that the patient soon becomes comatose. Even though this advanced stage is reached, a certain number of cases may yet recover, and this would appear

to depend largely upon the volume of the transfusion in the first place. Recovery is marked by a large diuresis and a return of the blood urea to within normal limits.

It is not uncommon for a purpuric rash to make its appearance at the peak of the illness.

The different possible results of a wrong group transfusion may be represented thus:

Transfusion of Incompatible Blood

Acute *haemolysis* of donor's cells (acute haemolytic reaction)

Clinical picture of severe shock

Death during or soon after transfusion OR Survival from the immediate reaction

Interval phase

Renal phase

Death in uraemia

Diuresis and recovery

Recovery without ever progressing to the stage of renal failure if the amount of blood transfused is small

Massive *agglutination* of donor's cells with cerebral or cardiac embolism

Instantaneous death

As the writer has had the good fortune never to have seen incompatible blood transfused, an eyewitness account of a case seen and reported by Bordley (1931) will be given in detail

The case was one in which the donor was of group A and the recipient was of group O. Fresh citrated blood was used for the transfusion. The events that accompanied the injection of blood were as follows:

Immediate Reaction

During the introduction of the first 20 c c. the patient complained of creepy sensations all over her body. She said that her head felt full and tight as though it were going to burst. The subjective change seemed so definite that five minutes were allowed to pass before the injection was continued. *A second 20 c c. was introduced cautiously. The patient* complained of a severe headache. Her face became suffused; there was fullness of the veins of the neck; respiration grew shallow and laboured; she became nauseated and soon vomited. It was decided to discontinue

the transfusion and the needle was removed from the vein After an interval of twenty minutes, the patient announced that she was 'feeling fine We were so confident of our blood matching that the transfusion was resumed and a further 40 c c were injected without incident There were no symptoms as the fifth injection was started Scarcely 10 c c , however, had been injected when the patient suddenly complained of lumbar backache fullness of the head, and faintness She became short of breath and cyanotic, the pulse rate rose rapidly and the beats could barely be detected at the wrist The transfusion was discontinued after a total of 90 c c had been injected A quarter of an hour after the end of the transfusion there was a violent *chill* and the patient had an involuntary stool After half an hour the rigor ended but cyanosis was still marked and respiration was rapid and deep There was considerable spontaneous bleeding from the vene puncture wounds in both arms which could be controlled by the application of pressure bandages

Interval Phase

After a night's sleep she felt fairly well At 5 a m and again at 8 a m on the following morning she voided 100 c c of coffee coloured urine, containing much haemoglobin albumin a few red blood cells, and no casts She felt better in the evening and ate a good supper During the next three days the *patient seemed to be recovering satisfactorily* The haemoglobinuria jaundice and vomiting, which had been striking features on the day after transfusion, subsided rapidly and finally disappeared

Renal Phase

Oliguria which had been marked since the transfusion gave way to complete urinary suppression From the fourth to the eighth day she was in a state of incipient uraemia culminating in generalized convulsions on the eighth day after the transfusion following which she became comatose On the morning of the ninth day she regained consciousness and though drowsy, was orientated Together with a symptomatic improvement on that day, the urinary suppression gave way to diuresis which on the tenth day amounted to 5 000 c c of urine in 24 hours As the diuresis progressed the patient cleared mentally and the blood N P N fell gradually to normal (Bordley, 1931)

Treatment

Before transfusion

Alkalinization of the recipient before a transfusion is a reasonable prophylactic measure in view of the observation made on the experimental animal that haemoglobin liberated by intravascular haemolysis is precipitated in an acid urine but remains in solution in alkaline urine

Unfortunately, in an emergency there is no time for extended preventive treatment, so that once again one must rely on that most important of all prophylactic measures—the direct compatibility test. If in addition to this test the first 20 c.c. of blood is injected very slowly—the so called biological test—we shall have experience of very few misfortunes.

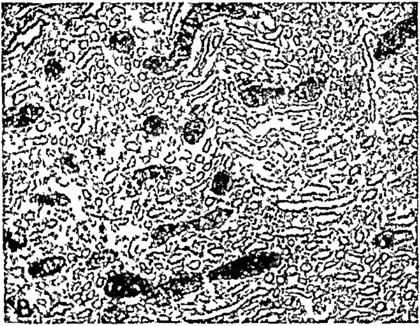

FIG. 21. (By courtesy of Goldring and Graefe.) A wrong group transfusion: the renal changes.

After transfusion.

By alkalinization. Alkalinization at this stage can do no harm, and by tending to promote a diuresis and so washing out the obstructing casts, may slightly relieve the intrarenal obstruction. Unfortunately once the haemoglobin has been precipitated as acid haematin, it is relatively insoluble but even so the pigment is more likely to be dissolved in an alkaline than in an acid urine. Clearly the earlier administration of alkali is begun, the better are the prospects of recovery.

The alkali should be administered as potassium citrate and sodium bicarbonate by the mouth, and as sodium bicarbonate

intravenously The general treatment of the patient will include the application of heat and cupping to the loins

Many other procedures have been suggested and been reported as successful in isolated cases

Transfusion of Compatible Blood

Hesse and Filatov (1933) who claim that the renal suppression is ischaemic in origin say that retransfusion as soon as possible with compatible blood is the most satisfactory method of treatment following an incompatible transfusion They believe that the transfusion acts by relieving arterial spasm produced by the toxic breakdown products of haemoglobin Amounts of 200 to 300 c c of blood are said to be sufficient for the purpose of detoxication

Decapsulation of both kidneys following transfusion anuria was associated with recovery in a case reported by Bancroft (1925) and another reported by Younge (1936) recovered following decapsulation of the right kidney

Irrigation of the renal pelves with hot water phlebotomy and intravenous fluids both hypotonic and hypertonic have been associated with recovery in their turn but as DeGowin (1938) points out it is noticeable that some cases recover spontaneously while others die in spite of the therapeutic measures

The Cause of Suppression of Urine

The mechanism of production of the anuria seems now to be well understood largely due to the work of Yorke and Nauss (1911) Ross (1932) and Fairley (1934) on cases of Blackwater fever the experimental work of Baker and Dodds (1925) on rabbits and the confirmation of this work by DeGowin Osterhagen and Andersch (1937) on dogs Their conclusions are embodied in what is now commonly called the obstructive theory

Before discussing the actual method of obstruction however it will be well to consider first what part of the transfused blood is responsible for the renal damage Baker (1937) in a valuable paper considers this problem under the following headings

1 *Is it the plasma or the corpuscles?* The answer to this is given by a case reported by De Gowin and Baldridge (1934) where haemoglobinuria jaundice and a fatal suppression of urine followed transfusion with

washed red corpuscles This case and the experiments of Yorke and Nauss (1911) and Baker and Dodds (1925), in which suppression of urine in rabbits was produced by lysed washed red cells prove definitely that the corpuscles are responsible for the damage

2 *What part of the corpuscles is responsible?* The corpuscles can be separated into the haemoglobin and the stroma and in experiments on rabbits it was found necessary to remove the stroma by filtration in order to avoid capillary emboli and thrombosis in the lungs which caused immediate death in these animals when whole lysed corpuscles were injected intravenously In these experiments, therefore, urinary suppression and nitrogen retention was produced by the haemoglobin fraction alone We can say then that haemoglobin liberated by intra vascular haemolysis of the transfused corpuscles is responsible for the renal damage

The obstructive theory.

The workers already referred to believe that there is a mechanical blockage of the renal tubules by blood pigment, so called 'haemoglobin infarction'. According to experiments by Baker and Dodds on rabbits (1925) *the donor's blood* is haemolysed and the blood pigment is excreted by the kidneys where the haemoglobin is precipitated by the acid urine as acid haematin This precipitate mechanically obstructs the tubules causing uraemia if a sufficient number of nephrons is involved Clinically the obstructive theory is supported by the fact that the urinary suppression dates from the onset of the haemoglo binuria In addition, the fact that lumbar pain is the earliest symptom fits in with the view that distension and obstruction occur early on, causing the pain Although jaundice and haemo globinuria usually occur, their absence must not be allowed to negative an intravascular haemolysis The jaundice, unless it is looked for in the early period, may be missed, as it rapidly disappears, and it is quite possible that if the precipitation of the haemoglobin in the renal tubules was rapid and complete, no soluble pigment would escape from the kidney even though some urine was excreted

The mechanism of intrarenal obstruction

The haemoglobin derived from the haemolysed red blood cells circulates as oxyhaemoglobin and is filtered through the glomeruli as such In the tubules, provided that there is a pH

of 6 or less and a concentration of NaCl exceeding 1 per cent (Baker and Dodds 1925) the oxyhaemoglobin is converted into methaemoglobin and ultimately into acid haematin which appears to constitute the bulk of the precipitate blocking the lumina If the urine is alkaline when the oxyhaemoglobin enters the tubules these changes do not take place and the oxyhaemoglobin is excreted unaltered For this reason death in rabbits at any rate may be prevented by administering alkalis intravenously and by mouth

The toxic theory

Having narrowed down the causative agent to the haemoglobin factor there remains to be disproved the theory that free haemoglobin is toxic to the kidneys In this connexion it has been suggested that the production of a toxic nephritis by the circulating haemoglobin is the primary and most important effect of an incompatible transfusion or alternatively that the haemoglobin has a toxic vasoconstrictor affect upon the renal vessels (Mason and Mann (1931) Hesse and Filatov (1933) and so limits excretion by diminishing glomerular activity The Russian workers also believe that the lumbar pain is due to the spasm of the renal arteries and is an ischaemic symptom

The toxic theory has been challenged by Baker (1937) who says The outstanding fact which cannot be explained by *any* of the suggested alternatives is that under certain conditions a gross haemoglobinuria may occur without any evidence of renal damage whereas under other conditions the secretion of urine is suppressed In other words it is not reasonable to suppose that haemoglobin may be toxic on some occasions and non toxic on others

In man haemoglobinuria without appreciable renal damage may occur in

(i) Paroxysmal haemoglobinuria

(ii) Blackwater fever particularly in cases treated with alkalis Experimentally also a harmless haemoglobinuria was produced in man by Sellards and Minot (1916) after the intravenous injection of haemoglobin and in animals normally secreting an alkaline urine—for example rabbits—the transfusion of filtered haemoglobin solutions is harmless On the

other hand, in animals secreting an acid urine, the injection of haemoglobin produces a renal suppression

It would seem that the part played by toxins in cases of incompatible blood transfusion is probably a secondary and minor one Some toxins may possibly be derived from broken down haemoglobin products, and by circulating exert a secondary effect upon the liver and other organs, or may it not be that these viscera are affected as a result of the long standing suppression, by retained products of metabolism normally excreted in the urine ?

DIAGNOSTIC PROCEDURES FOLLOWING A SUSPECTED WRONG GROUP TRANSFUSION

1 *Spectroscopic* examination of the plasma for extracorpuscular oxyhaemoglobin and methaemalbumin and chemical examination for hyperbilirubinaemia by the van den Bergh test

2 *Urinary* examination this should include spectroscopic examination for oxyhaemoglobin and methaemoglobin, and a microscopical examination of the centrifuged brown deposit for red blood corpuscles and casts The total volume of urine passed should be carefully recorded

3 *Re grouping* of donor and recipient with
   (a) Stock serum—high titre
   (b) Stock cells

4 *Re cross Matching* of donor and recipient
   (a) Naked eye
   (b) Hanging drop

Diagnostic Confirmation

The presence of haemoglobinaemia and haemoglobinuria constitutes the most reliable evidence of a haemolytic reaction

1 *Haemoglobin and its derivatives in the plasma* (Fairley)

In collecting blood for this purpose care must be taken to prevent plasmolysis or reduce it to a minimum A dry syringe and needle should be used and blood, obtained by venous puncture, slowly run into a sterile tube containing oxalate solution or heparin, this should be gently inverted two or

three times to ensure mixing. Subsequently the specimen is centrifuged, the plasma carefully pipetted off from the sedimented corpuscles and examined spectroscopically. If oxyhaemoglobin is present the characteristic spectroscopic picture is seen with a sharply defined α band in the yellow and a β band in the green. An additional band in the red portion of the spectrum is also generally evident a few hours after the onset of any severe intravascular haemolysis such as occurs in blackwater fever. Fairley and Bromfield (1937) have shown this is due to *methaemalbumin* (pseudo methaemoglobin) which may need to be differentiated from two other blood pigments also giving an α band in the red portion of the spectrum, namely, methaemoglobin and sulphaemoglobin. The methods of doing so are epitomized in the Table below.

Differences between certain Blood Pigments in man producing a brown plasma and presenting an Alpha band in the Red portion of the Spectrum (Fairley, 1939)

	Test	Methaemoglobin	Methaemalbumin (Pseudo-methaemoglobin)	Sulphaemoglobin
1	Location	Intracorpuscular	Intracorpuscular	Extracorpuscular
	Position of α band	6,300 Å	6,230 Å	6,180 Å
2	Concentrated ammonium sulphide	Dispersed (Reduced haemoglobin)	Dispersed (Haemochromogen)	Unaltered
4	Ammonium sulphide (10 per cent.)	Dispersed	Unaltered	Unaltered
5	Stokes's reagent (fresh)	Dispersed	Unaltered	Unaltered
6	Sodium hydrosulphite ($Na_2S_2O_4$)	Dispersed (Reduced haemoglobin)	Dispersed (Haemalbumin)	Unaltered
7	Hydrogen peroxide (10 vols.)	Dispersed	Persists for some time	Slowly dispersed

Actually the α band of methaemalbumin (6230 Å.) lies midway between that of methaemoglobin (6300 Å.) and sulphaemoglobin (6180 Å.) but their identification spectroscopically is difficult unless a Hartridge reversion spectroscope is used. However, the addition of a few drops of concentrated ammonium sulphide to the plasma leaves the spectrum of sulphaemoglobin unchanged, whereas that of methaemoglobin is converted into reduced haemoglobin and that of methaemalbumin into a typical haemochromogen. A few drops of a weak solution of ammonium sulphide (10 per cent.) or of Stokes's reagent

disperse the spectrum of methaemoglobin but not that of methaemalbumin or sulphaemoglobin By these and other chemical means, summarized in the Table, these three pigments can be *readily* differentiated and identified

Haemoglobin and its derivatives in the urine

The presence of oxyhaemoglobin and methaemoglobin in the urine is a valuable indication of intravascular haemolysis It may, however, be absent in mild cases of haemolysis where the renal threshold for haemoglobin has not been exceeded or when there is only a transient hoemoglobinuria and the first specimen, containing much of the excreted pigment has been discarded without examination This may readily happen where the nurse has not been warned of such a possibility Also, in severe cases where the potient rapidly becomes onuric omission to examine the early specimens may preclude the possibility of examining any

If the urine is bright red in colour it contains oxyhaemoglobin and is generally alkaline in reaction More frequently it is claret or porter coloured then methaemoglobin is found and the reaction is generally acid Both these pigments are readily demonstrated spectroscopically, but in milder cases it is advisable to examine thick layers of urine (5–10 cm) before deciding that blood pigment is absent A brown precipitote containing debris and granular casts, but not red blood corpuscles, is very characteristic of the severer cases with methaemoglobinuria Its brown colour is regarded by some as due to acid haematin derived from methaemoglobin

The fate of the circulating haemoglobin may be conveniently considered at this stage I am indebted to N H Fairley of London for the substance of the account which follows This incorporates his recent important contributions to the subject of plasma pigments

The Fate of Extra corpuscular Circulating Haemoglobin

Following a severe intravascular haemolysis such as may be encountered in incompatible transfusion, three different mechanisms for the disposal of extracorpuscular haemoglobin

may come into play (1) If the renal threshold be exceeded, oxyhaemoglobin, and generally methaemoglobin as well, appear in the urine The quantitative studies of Yorke, Murgatroyd, and Owen (1930) in blackwater fever indicate that not more than 10 per cent of the extracorpuscular haemoglobin derived from the intravascular haemolysis of red cells is excreted in the urine (2) Part of the circulating oxyhaemoglobin is absorbed by the cells of the reticulo endothelial system and converted finally into bilirubin which always circulates in the blood in increased quantity in intravascular haemolysis According to Lemberg (1937) verdohaemochromogen and biliverdin form essential intermediary stages and are precursors of bilirubin in this type of haemoglobin katabolism (3) The remainder of the haemoglobin not disposed of by these two mechanisms persists in the circulation where it ultimately splits into haem and globin the haem is oxidized to haematin, which as Fairley (1938) has recently shown couples with serum albumin to form a new pigment—methaemalbumin

Methaemalbumin

Methaemalbumin appears to be produced in all severe cases of intravascular haemolysis including incompatible blood transfusion and in the past has been confused with methaemoglobin owing to its somewhat similar spectroscopic appearance and chemical behaviour It is not a threshold substance for the kidney and is not found in the urine

Fairley (1939) recently reported that following intravenous injections of haematin in man and monkeys methaemalbumin was immediately produced, and Rimington (1939) working on the same subject demonstrated a marked increase in the porphyrin content of the stools following haematin injections It would appear from this recent work that methaemalbumin is mainly dealt with by the liver giving rise to an increased excretion of porphyrins which are known to be excreted in larger amounts in the haemoglobinurias and certain haemolytic anaemias

Post mortem Appearances

The post mortem appearances are fairly constant and typical and have been described in detail by Bordley (1931), Turnbull

(1936) Witts (1929) Baker and Dodds (1925), Payne (1934) and Plummer (1936) The renal changes which are bi lateral are characterized by

The Kidneys

Naked eye

The naked eye appearances are variable and not very distinctive

The *Kidneys* are usually enlarged and swollen This appears to be produced in part by oedema and cellular infiltration of the interstitial tissue and in part by the dilated and degenerated tubules

The *Cortex* as a rule is enlarged and congested It may be pale if there is marked tubular degeneration

The *Medulla* is typically striated with reddish brown markings due to the deposits of the granular material in the collecting tubules

The *Renal Pelvis* may be pale or speckled with petechial haemorrhages

Microscopic

The **lumen** of the proximal tubules tends to be collapsed but the collecting tubules are filled with a granular debris the colour of brown sugar This *haemorrhagic reticulum* entangles numerous red cells leucocytes and desquamating epithelial cells

The exact chemical nature of the granular debris has not yet been determined but that it is certainly a haemoglobin derivative is proved by the fact that it gives a positive benzidine reaction for organically combined iron although it does not give the prussian blue reaction for inorganic iron

The **lining** of the tubules is degenerated in places elsewhere there is simply a cloudy swelling There are no necrotic or fatty changes in the lining epithelium and no evidence of an inflammatory process in the form of round cell infiltration Cellular infiltration only occurs in the late stages and is confined to the interstitial tissues The other kidney changes are less constant Bowman's capsules are variously described as being dilated or collapsed The degree of dilatation of the tubules and of Bowman's capsules possibly depends on the extent and level of the

obstructing precipitate If the obstructing debris extends as high as the second convoluted tubule (Baker and Dodds first case) it is likely that Bowman's capsules will be distended if it is confined to the lower parts of the collecting tubules (Baker and Dodds second case) the proximal part of the system may show no sign of distension It must also be remembered that only a certain proportion of the nephrons or functional units of the kidney are working at any given time

The liver sometimes shows central necroses and other organs such as the lungs stomach and duodenum may show petechial haemorrhages which suggest that though the kidneys may be primarily involved the reaction is a more generalized one than is generally supposed

The difficulty is that only very few post mortem examinations have been made on this condition and rarely has the opportunity of more than one such autopsy come the way of any single observer

Prognosis

Once the immediate reaction has passed the prognosis would appear to depend upon

1 The amount of incompatible blood introduced (Bordley, 1931)
2 The particular sensitivity of the individual to the products of the interaction
3 The existing state of the kidneys at the time of the transfusion (Brines 1930)
4 The severity of the disorder for which the transfusion was given together with the general health of the patient

In a series of seventeen cases reported by Bordley there was no instance of death occurring following the delayed reaction in patients receiving less than 350 c c No case receiving more than 540 c c recovered These figures relate only to the prognosis for the delayed reaction since theoretically 10 c c may be enough to produce an acute haemolytic response with collapse from which the patient may not recover There is thus a reasonable chance that if incompatible blood is given it will not produce a fatal reaction and this is particularly unlikely if (1) the operator is on the watch for the classical early symptoms already emphasized, and (2) the amount introduced is less than 300 c c

Mortality.

It is very difficult to obtain accurate figures relating to the mortality from blood transfusion, particularly as the tendency is to report deaths due to wrong group transfusions only My own impression is that *deaths from circulatory failure form a very much larger group*, but these cases only rarely find their way into the literature For this reason the following table probably considerably under estimates the number of deaths which should be directly attributed to blood transfusion

Reported by	*Year*	*Number of transfusions*	*Number of deaths*	*Percentage of deaths*
Brines	1930	4 000	2	0 05
DeGowin	1938	3 500	7	0 2
Polayes and Morrison	1932	1 500	9	0 9*
Watts	1929	3 430	5	0 14

* 1 000 *patients were transfused and the percentage fatalities calculated on* this figure

Investigating the Cause of a Reaction

If the reaction is haemolytic in type it may be due to

1 *Wrong grouping* of the donor or recipient or both

To investigate this possibility the potency of the typing serum should first be confirmed, and then the grouping of both donor and recipient repeated with stock serum *and stock cells* Too often retyping is carried out with stale serum and stock cells are not used at all A sample of the *recipient's* serum should be obtained at the earliest possible opportunity and examined spectroscopically for oxyhaemoglobin and methaemalbumin If the grouping is correct beyond doubt it is possible that the reaction may be due to

2 The interaction of an *accessory agglutinin* (C) *agglutinogen* (γ) pair of factors This coincidence is possible at the primary transfusion but is more likely to occur at a subsequent transfusion particularly if *the same donor is used again*

In these circumstances the cross test should be repeated when it will reveal the incompatibility Further confirmation of the presence of such an accessory agglutinin can be obtained by putting up the recipient's serum with group O cells when agglutination will be found to occur in a certain proportion of cases (Group O cells do not normally contain any agglutinogen factor) By absorbing the normal iso agglutinin in the *recipient's serum by exposure to the appropriate red cells the anomalous* agglutinin could be isolated and studied

In the case of a retransfusion reaction following the use of a different

donor it is more likely that the reaction is due to the presence of anti M (or N) agglutinins in the recipient's serum In this case also the cross test will show the incompatibility The presence of the M or N factor in the donor is readily confirmed by the use of immune anti M or N sera

3 The use of a *high titre donor* of different group to the recipient It is possible that in these circumstances the contained agglutinins have caused haemolysis of the recipient's cells

In such a case the titre of the agglutinins in the donor's serum should be estimated Reactions in these circumstances are most likely to occur when a group O is given to a group AB

The more anaemic the patient the more *liable* is the incoming serum to give rise to trouble

4 In certain circumstances the blood may be already partly haemolysed before it is introduced into the patient

(i) Overheating of the blood The temperature of the water surrounding the blood-container should never be raised above 104° F or the corpuscular envelopes may be ruptured

(ii) Freezing the blood If the blood has been kept at freezing point or below haemolysis of the cells will occur on thawing For this reason the average domestic refrigerator is unsuited to the storage of blood

(iii) Prolonged storage Blood corpuscles which have been conserved beyond a certain time increase in fragility and readily haemolyse At present the limit of safe storage in citrate solution appears to be only about 8 days and rather longer when glucose is added to the citrate

(iv) Mixing the blood If the blood of two or more donors is allowed to mix in the reservoir before infusion there is the risk that irregular agglutination will take place

(v) Vigorous stirring during collection or agitation during transport

The commonest cause of an obscure haemolytic reaction is *incorrect primary grouping*

If the reaction is febrile in type and particularly if a considerable percentage of all transfusions is being followed by this type of reaction it will be well to review the possible causes The cause may be found in

1 *The apparatus and solutions* The cleaning and sterilizing of the different parts may be imperfect Sour will turn whatever you pour—in vessel not quite clean before Rubber bungs needles flasks and so forth should be examined for evidence of old blood-clot and instructions given as to how this may be removed Tubing may give rise to trouble in two ways New tubing usually contains powdered French chalk in the lumen and tubing which has been used before may contain dried blood Both can be satisfactorily removed by boiling with soda The method of preparing the solutions—citrate and saline—should also be investigated with special reference to the technique of distillation (purification) The duration and conditions of storage and concentration and dosage of the citrate should also be examined

2 *In the technique* Here the inquiry may be directed along these lines

(*a*) *In collecting the blood* Was the blood adequately citrated? *Minute coagulative changes are possible if the dose is too small* On the other hand, if the dose is excessive, osmotic and toxic effects may be produced Was the blood violently agitated or stirred during collection or transit? *Was there any possibility of contamination by droplet infection—talking, laughing or coughing?*

(*b*) *In transfusing the blood* Was the *temperature* of the blood carefully controlled? In a relatively rapid transfusion the introduction of blood at a temperature below that of the patient is particularly liable to be followed by a rigor The clinical picture will be exaggerated if cold agglutinins are present in addition

Was the *patient exposed* for an unduly long time while the needle or cannula was being inserted? *I have repeatedly observed that when the* introduction of the blood has been held up by technical difficulties the frequency of a post transfusional chill or rigor is high

3 *In the patient* It is well to remember that certain illnesses are more commonly associated with reactions than others in general medical rather than surgical illnesses the chronic sick rather than the acute

If the reaction is anaphylactic or allergic in type

The anaphylactic and allergic reactions are essentially inter sera reactions as opposed to the haemolytic which is a serum cells reaction It is important to bear this in mind in seeking for the cause

The donor s and recipient s history in relation to this subject must be carefully examined and individual idiosyncrasies of an allergic nature sought for The question of food sensitivity and the possibility of a culpable circulating substance in the donor s serum at the time of the transfusion will have to be excluded Contacts made by the donor to which the recipient is also sensitive may also afford an explanation of an obscure reaction

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CHAPTER IX

THE PRINCIPLES OF DOSAGE IN BLOOD TRANSFUSION

THE principles of dosage outlined below are presented somewhat dogmatically The alternative was to be vague and uncompromising I have tried to mellow the full blooded quantitative approach to the determination of dosage without destroying its essentially constructive basis, but the subject is by no means as simple as it is set out Paradoxically blood transfusion after a severe haemorrhage actually depresses the bone marrow, and it may be that in certain cases of chronic anaemia too massive a transfusion will defeat its own object by removing the stimulus to new blood formation

For purposes of description, although this rule must not be applied too rigidly, there are two main 'sizes' of blood transfusion, the small volume transfusion of approximately 600 c c. and under, and the larger volume transfusion which is given at a drip rate over a prolonged period of time and involves the use of more than one donor The decisive factor in determining which of these two types of transfusion will be used is the presence, or absence, of anaemia But it has constantly to be remembered that blood transfusion is only a *temporary* method of making good a deficiency of red corpuscles

In the absence of anaemia. In the absence of anaemia the blood is usually given (i) as a haemostatic, (ii) to increase resistance, or (iii) in the treatment of shock In these circumstances a small volume transfusion of 200 to 600 c c is all that will be necessary or of benefit, for in conditions unassociated with an anaemia, it has been widely observed that no additional advantage is to be obtained from transfusions of larger volumes Examples of conditions for which a small transfusion is indicated are haemophilia, thrombocytopenic purpura, and sepsis It may also be of value when administered to convalescent patients who are not progressing as they should be

In the presence of anaemia. In the presence of anaemia, whether acute or chronic, it has for long been the custom, regardless of the stature of the patient or the degree of the

anaemia to transfuse an arbitrary volume of blood. This is usually a pint—*an empirical quantity having no clinical or even mathematical significance* arrived at by considering the quantity of blood which can safely be withdrawn from one donor rather than the amount which should be given to the patient.

Attention was drawn to this empiricism in 1935 in an important paper by Marriott and Kekwick. They suggested that the usual transfusion of 500 c.c. given to a case of anaemia was probably quite inadequate since if we assume the total blood volume in a normal adult to be 5,000 c.c. a transfusion of 500 c.c. can and does raise the haemoglobin of the recipient by only 10 per cent. and in a patient with a really low percentage of haemoglobin this will be of little benefit. They therefore sought to establish the principle that the quantity of blood to be transfused in anaemic cases should be regulated with a view to restoring the haemoglobin to within normal limits.

THE PROBLEM OF DOSAGE

In the treatment of a severe anaemia the aim should obviously be the restoration of the blood count to normal, and the question arises as to whether this is best brought about by a full quantitative replacement of red cells by transfusion or whether the transfusion should aim at a partial replacement only, the remaining deficit being made up by other means. The principle of the large volume transfusion—that is the quantitative replacement of red corpuscles—is not intended to be applied wholesale to all types of severe anaemia. For example it is clearly unnecessary to replace red corpuscles quantitatively in those anaemias which will respond to iron or liver medication. My own experience suggests that attempts to achieve *full restoration* of the haemoglobin to within normal limits are unnecessary in acute anaemias and unsafe in the chronic forms.

On the other hand it is very important that we should not revert to the generally *inadequate* dosage that has been so widely employed up to the present time.

The optimum dosage in the severe anaemias would seem to be between the two extremes that have been described. The small volume—pint size—transfusion is insufficient in these cases

and the large volume quantitative replacement of blood is unnecessary

A Guide to Dosage

Severe anaemias of rapid development — Acute anaemias

Although the haemoglobin deficit when this is known forms the working basis from which the dosage will be calculated in all anaemias it follows from what has already been said that it will *generally be unnecessary to make up by blood transfusion* the whole of this deficit The extent to which the haemoglobin should be raised by blood transfusion will depend essentially upon the urgency of the need for red corpuscles in other words, the clinical state of the patient Thus after a sudden severe haemorrhage it will be important to raise the haemoglobin to a level at which the physiological powers of accommodation may become effective—this as Keith (1919) has shown is in the neighbourhood of 75 per cent of haemoglobin The regenerative power of a healthy individual who has suffered a severe haemorrhage—provided some considerable portion of the lost blood is restored—will be more than equal to making up the balance without undue strain upon the blood forming organs

Severe anaemias of gradual development — Chronic anaemias

In those anaemias on the other hand in which there is no particular urgency for a rapid return of the haemoglobin to normal the dosage of blood will depend upon the extent to *which the patient may be expected to respond to iron or liver* therapy before and after the transfusion

The temporary type of chronic anaemia

In attempting to assess the dosage in the chronic anaemias we must remember that blood transfusion is a therapeutic remedy not without risk and we should aim at raising the haemoglobin only so far as is necessary and of advantage to the patient The *optimum level* as stated above is that from which one can reasonably expect to restore the haemoglobin to normal by iron and other means In a chronic anaemia of long standing

I would aim at transfusing back to 75 per cent haemoglobin and in one of shorter duration when the haemopoietic system is generally less exhausted to 60 per cent haemoglobin By the old standards these figures would have been much lower by the quantitative standards somewhat higher

After transfusion it will nearly always be possible to raise the haemoglobin to within normal limits by *iron* if we are not in too much of a hurry to allow a proper course of this drug to take full effect One of the first principles of medicine is to employ the natural method of cure and it is surprising how effective this can be in these particular circumstances if it is conscientiously carried out In some cases if the patient is seen in the Out patient department with anaemia from a chronic moderate menorrhagia for instance it will be possible by instituting iron treatment with rest in bed if necessary to prepare the patient for operation preferably some six weeks later without a transfusion at all

The permanent type of chronic anaemia

If the anaemia is of the *permanent type* such as aplastic anaemia which does not respond to iron or liver it will be necessary to rely entirely upon blood transfusion The optimum level for each patient will have to be found by trial

Some authorities would maintain the level at 60 per cent others as high as 80 per cent the question is still unsettled

Severe anaemias requiring immediate operation

In recent or long standing severe anaemias requiring immediate operation a safe operative level to aim at will be 75 per cent of haemoglobin

Haemoglobin raised by stages

Although the haemoglobin may be very considerably raised by the drip technique without disturbing the blood volume or overloading the circulation it is not in all cases in the best interests of the patient to do this in one stage

It is a good rule not to raise the haemoglobin by more than 30 per cent at a time—that is to say, no single transfusion should exceed approximately 1 500 c c in volume Amounts greater than this should be given in two or more stages

Indications for large volume transfusions

Relatively large volume transfusions are primarily *indicated* in severely anaemic states requiring immediate operation—that is to say, in individuals in whom it is necessary to raise the blood to a safe operative level rapidly, for example, a bleeding peptic ulcer or bleeding uterine fibroids

Large volume transfusions are *contra indicated* in those anaemic cases in which the time factor is not so pressing and in which it will be possible to restore the blood count, partly by a small transfusion and partly by iron or liver therapy

THE CALCULATION OF THE DOSAGE IN ANAEMIC CASES

The basis on which the dosage is computed will depend upon whether the haemoglobin level is stabilized or not In the chronic anaemias the haemoglobin level at any given time can be accurately determined, and the dosage can then be calculated In acute anaemias however, for some hours after the haemorrhage the blood remaining in the circulation is being diluted by the tissue fluids so that the true haemoglobin level cannot be estimated In these cases the dosage must be determined by some other means

When the haemoglobin level is stable

In the chronic anaemias and all cases of severe haemorrhage, 12 hours or more after the bleeding has stopped the dosage can be based on the haemoglobin deficit To calculate the volume of blood that will be required the following data must be known

1 The haemoglobin level of the patient to be transfused

2 The volume of blood that may be expected on transfusion to raise the haemoglobin level of the recipient by a constant percentage

If we assume that the total blood volume of the average adult is 5,000 c c and that the cells are carrying a full complement—100 per cent of haemoglobin—then one tenth by volume of this—namely, 500 c c —will correspond to 10 per cent haemoglobin For practical purposes in determining the dosage it may be assumed that a transfusion of 500 c c will

raise the haemoglobin of the recipient by 10 per cent The normal range for the blood volume is 5 000 to 6 000 c c , so that rather more blood will be required by heavily built people

Let us take an imaginary patient with chronic anaemia requiring immediate operation suppose the haemoglobin is 30 per cent —a safe operative level to aim at will be 75 per cent —in other words the haemoglobin will have to be raised by 45 per cent According to the data above this patient will require 2 500 c c Transfusions of this magnitude must be given in two or more stages

When the haemoglobin level is unknown—in acute haemorrhage

This will apply to cases of haemorrhage seen immediately after the blood loss and up to approximately 12 to 24 hours later by which time the blood volume–tissue fluid balance will be stabilized

It has been said that haemoglobin estimations immediately after a severe haemorrhage are of little value and it is clear that blood volume estimations at this stage are impracticable (see discussion p 137) and that actual measurement of the blood lost may not be possible What basis then is left for computing the dosage? This must be determined on the clinical aspect of the case Keith (1919) has pointed out that if serious symptoms are present it may confidently be assumed that between one quarter and one half of the blood volume has been lost A transfusion of between 750 c c and 1 500 c c will therefore be required to bring the haemoglobin back to the 75 per cent mark (p 140) As the transfusion slowly proceeds more accurate estimations of the haemoglobin level will be possible so that the initial dosage proposed can be reassessed and altered if need be

THE PRINCIPLES GOVERNING THE RATE OF INTRODUCTION

Of the two points of fundamental importance in connexion with the administration of the blood in transfusion namely the rate of introduction and the quantity introduced it is my own opinion that the rate of introduction is the more important

I have in this book avoided the term 'continuous drip transfusion', as there has been a tendency to interpret this phrase as synonymous with transfusions of large volume I personally believe that almost all transfusions should be continuous drip transfusions, that is in the sense that the blood is administered *at a drip rate*, and it is my own practice to 'drip' every patient that I transfuse, with the exception of those who need a rapid replacement of red corpuscles because of a severe haemorrhage —and these do not amount to as many as one in ten

It may be argued that there is not time to give all transfusions at a drip rate In practice I find that they take up less time than the more rapid method which requires the operator's presence throughout the transfusion Once a drip transfusion has been started it can be left to give itself It may also be felt that a drip rate is unnecessary in the majority of transfusions On the contrary, I believe that if we are to make blood transfusion safer than it has been in the past this is the most important single measure towards achieving our object and for these reasons

(i) The risk of overloading the circulation is minimized In anaemic cases of long standing the cardiac muscle also becomes anaemic so that the mechanical efficiency of the heart is greatly impaired The rapid introduction of even a small volume of fluid in these circumstances may precipitate heart failure I have seen this happen on one occasion after 400 c c had been injected the patient developing acute pulmonary oedema a few minutes after the transfusion had been completed and dying within half an hour

(ii) Reactions in the form of chills or rigors are fewer Some grade of reaction is almost invariable following transfusion by rapid methods in a severe medical anaemia If this reaction should take the form of a rigor the extra mechanical strain thrown upon an already weakened myocardium may produce acute circulatory failure My own reaction rate (rigors) since I have adopted the drip rate has dropped from 20 to 11 per cent

(iii) *Interaction* between the patient's corpuscles and the agglutinins in the incoming serum is slowed up If blood

is introduced rapidly into a vein, the serum fraction mixes immediately with the venous blood of the recipient and is very little, if at all diluted until it has been redistributed by the heart throughout the systemic circulation If the agglutinins in the transfused serum are for any reason incompatible with the recipient s cells agglutination of these cells may be produced If, however the blood is being very slowly introduced the incoming serum agglutinins will be immediately diluted by the comparatively large volume of blood in the vein and even if incompatible it is unlikely that they will exert a maximum effect Furthermore at this slow rate it is likely that the bulk of the agglutinins introduced will be immobilized by absorption

THE RATE OF INTRODUCTION

In adults the exact rate of introduction should depend upon such considerations as whether the transfusion is one of small or large volume the urgency of the demand for oxygen carrying cells the duration of the anaemia the mechanical efficiency of the heart muscle and upon whether the case is still bleeding or not

In Large Volume Transfusions

In large volume transfusions the rate of introduction should depend on whether the patient is bleeding or not

In non-bleeding patients

In non bleeding patients Marriott and Kekwick (1935) have found by experience that a safe rate of introduction of the blood is 500 c c in 4 hours This is another way of saying, a rise of the haemoglobin proportion by 10 per cent 4 hourly In non bleeding adult patients this can be achieved by maintaining a drip rate of 40 drops a minute A transfusion of, say, 1 500 c c should therefore take not less than 12 hours

In bleeding patients

In bleeding patients the rate of introduction must be accelerated to keep pace with the loss of blood The same—40—or a slightly faster rate—up to 60 drops a minute—should be used to start

with Repeated haemoglobin estimations will indicate how fast the blood should be allowed to flow Clearly if consecutive readings show a fall in haemoglobin percentage the pace will have to be quickened

In Small Volume Transfusions

It should be borne in mind that a small volume transfusion is not necessarily synonymous with a rapid transfusion It may be but the state of the heart must always be assessed first A 500 c c transfusion which can safely be given in less than 30 minutes to some one with a normal heart *will precipitate heart failure* in an individual whose myocardium has for a long time been incompletely nourished with blood or weakened by toxins This question is more fully discussed in Chapter VIII I find that less than one in ten of the patients that I transfuse can safely be given this rapid type of transfusion

In the few cases in which the myocardium is normal blood may be introduced in small transfusions to adults at the rate of 100 c c in 5 minutes At this rate a 600 c c transfusion will take half an hour This is the maximum rate permissible To be on the safe side it is my own practice to take 45 minutes to give a pint of blood to this type of patient

Such small volume rapid transfusions will usually be given

(i) In urgent cases of severe anaemia due to haemorrhage—provided the bleeding has been arrested by ligature or suture

(ii) In a few cases of mild chronic anaemia of recent development in which it is not required to raise the haemoglobin by more than 10 to 12 per cent This will apply particularly to convalescent cases—whether medical or surgical—which have come to a standstill in their progress and in which the transfusion is being given as a general stimulant and tonic

WEIGHTS AND MEASURES

One pint corresponds to 568 c c or 20 fluid ounces

100 per cent haemoglobin (Haldane) corresponds to 13 8 gm per cent haemoglobin

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CHAPTER X

THE CONTRA-INDICATIONS TO BLOOD TRANSFUSION AND SOME PRECAUTIONS

ALTHOUGH absolute rules cannot be laid down forbidding the administration of blood to any given patient there are circumstances in which transfusion is usually contra indicated and occasions when it will be wise to review very carefully the existing conditions and prognosis before deciding to give blood

Cardiac failure or disease is the most important contra indication It sometimes happens however that for example a girl with an uncompensated mitral lesion requires transfusion as a result of an accident or an obstetric misadventure In these circumstances the transfusion should be given at a drip rate and possibly be preceded by a venesection

Transfusion in the presence of severe anaemia or gross sepsis

Severe chronic anaemia and gross sepsis are indications for rather than contra indications against transfusion but they are included in this section to draw attention to the care that must be taken in transfusing these patients if severe and possibly fatal reactions are to be avoided

It might be well to formulate a rule that these transfusions must be given at a *slow drip rate* There is no exception to this rule for the rapid introduction of blood into these patients if it does not produce heart failure from primary overloading of the toxic or anaemic myocardium will almost certainly be followed by a rigor and the onset of cardiac failure secondary to this

The direct test has to be made with care for the greater the anaemia the more marked will be the effect of minor degrees of incompatibility between donor and recipient Unfortunately, pseudo agglutination is very common in these cases and makes the determination of compatibility more difficult If the recipient's serum is diluted with a drop of normal saline there is usually no difficulty in coming to a decision (p 43)

Chronic nephritis

In a small proportion of cases following transfusion in which the blood groups of donor and recipient appear to have been compatible there has been a reaction of the renal type with anuria or oliguria In a few of these cases of unexplained haemolytic reactions there has been evidence of a pre-existing chronic nephritis (Brines 1930) It is reasonable to suppose that a damaged kidney will be more readily obstructed than a normal organ by a haemoglobin precipitate If this is so even a minor degree of haemolysis in a patient with diseased kidneys might be expected to produce a partial or complete anuria in such organs whereas a similar amount of deposit in normal kidneys would probably be insufficient to cause any noticeable alteration in function It must be remembered however that in many of the cases of unexplained haemolytic reaction producing renal symptoms there has been no evidence of any existing or pre-existing nephritis It may be that in certain individuals the kidneys are unusually sensitive to the products of a haemolytic reaction either because they are together with other organs part of a grave constitutional disturbance or because of some local allergic phenomenon

Blood transfusion These observations do not contra-indicate the transfusion of blood to individuals with a history of renal disease or damage but they emphasize the importance of careful direct compatibility tests before a donor is accepted It will also be wise to *alkalinize* the patient's urine prior to the transfusion

Previous severe reaction

Retransfusion of a patient who has had a rigor following a previous transfusion must always be a cause for anxiety both to patient and operator Precautions to take in retransfusing these patients will include introduction of the blood at a drip rate and the use of a different donor but the whole technique used at the previous transfusion should be critically reviewed and the method of preparation of apparatus and solutions investigated The subject is discussed more fully on p 74

Leukaemia.

It is difficult to know what to advise in the leukaemias In the *acute* leukaemias—myeloid and lymphatic—blood transfusion is, I think, contra indicated, for it may produce the most violent reaction and at the best can only bring about a very temporary improvement (Hart, 1938) From the humanitarian point of view transfusion can only be regarded as postponing death, and should there be a reaction the patient's condition will be even more distressing than before Transfusion possibly enables a patient to withstand X rays better

In the *chronic* forms, blood transfusion may bring down a temperature or lessen some of the anaemic symptoms, but it is only a palliative measure and should not be used without careful examination of the particular circumstances

Aplastic anaemia.

In those types of aplastic disease of the bone marrow which involve *all* the formed elements of the blood, blood transfusions should not be used unless there is some special reason for trying to prolong life for a few days or weeks, for instance to allow a relative time to return from abroad It is, however, not often possible to be certain that the aplasia is complete, and in such circumstances the patient should always be given the benefit of the doubt

In aplasia or hypoplasia involving only the erythrocytes, blood transfusion is the therapeutic remedy of choice This is discussed more fully on p **147.**

The allergic or protein sensitive recipient

In a patient who is known to be sensitive to certain substances it will be advisable to exclude as far as possible an unsuitable donor Intradermal injection of the donor's serum into the patient will help to pick out unsuitable donors In addition, in all doubtful cases ephedrine should be given in tablet form before the transfusion, and adrenaline should be at hand drawn up in a syringe in case it is required during the course of the transfusion (See also p 80)

Deficiency anaemias.

Blood transfusion is unnecessary in those anaemias in which the deficiency can be supplied in the diet or otherwise corrected

by some simple method of adjustment. Examples of these anaemias include:

1. **Iron deficiency anaemias.** These may be due to:

(a) *Deficient diet.* In *infants* such anaemias include those of twin births and prematurity, the nutritional anaemias of infancy due to a deficient intake of iron during the milk feeding period, the anaemia due to excessive prolongation of milk feeding, and the alimentary anaemia of infants past the milk feeding period.

In *adults* the iron deficiency anaemias include simple achlorhydric anaemia and chlorosis—the latter a very rare disease nowadays.

(b) *Deficient absorption.* Deficient absorption of iron is seen in coeliac disease and perhaps in intestinal infections, although in these cases toxaemia is also a factor in the causation of the anaemia.

2. **Haemopoietic factor deficiency anaemias.** This deficiency occurs in pernicious anaemia and the macrocytic anaemia of pregnancy. Neither of these diseases requires blood transfusion as a rule, as the response to liver therapy is generally so satisfactory. The occasions on which blood transfusion may be necessary are discussed on p. 150.

3. **Anaemias due to a double deficiency of iron and haemopoietic principle.** Most of these patients respond well to combined iron and liver treatment. In some of the cases in which there is an extensive gastritis, some degree of hypoproteinaemia may develop. In those instances in which this is associated with tissue oedema, a transfusion of blood or serum will give rapid relief.

4. **Endocrine and vitamin deficiency anaemias.** Hypothyroidism and cretinism may be associated with an anaemia. They respond well to thyroid extract but not to liver or iron alone. Deficiency of vitamin C is responsible for the anaemia of scurvy.

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CHAPTER XI

INDICATIONS

TRANSFUSION of blood may be used

To replace blood lost, destroyed, or chemically inactivated

To maintain life in aplastic diseases of the bone marrow

To increase resistance

To stimulate the bone marrow or other parts of the haemopoietic system

To increase the coagulating power of the blood

To replace or dilute toxic blood

To restore blood volume—in shock

To raise the serum protein content

THE INDICATIONS FOR BLOOD TRANSFUSION

The indications for blood transfusion are best considered in greater detail by tabulating according to the particular deficiency in the blood of the patient which the transfusion is intended to remedy Thus transfusion of blood may be required

To supply oxygen carrying red corpuscles when

1 Red blood corpuscles have been **lost** extravascularly by haemorrhage, whether acute or chronic

2 Red corpuscle formation is **insufficient:** this may be due to

(a) *Depressed* function of the bone marrow, as in

(i) Primary aplastic anaemia

(ii) Secondary or *symptomatic* aplastic anaemia due to such causes as prolonged irradiation by radium or X rays, acute and chronic infections, whether localized in the bone marrow or secondarily affecting the marrow through the toxins originating from some soft tissue focus

(b) *Disordered* function of the bone marrow

Pernicious anaemia

Macrocytic anaemia of pregnancy

3 Red blood corpuscles have been **destroyed** intravascularly by haemolysis This is seen in

A The *haemolytic* anaemias which may be due to

(a) *Infective toxic, and poisonous factors* These agents also tend to depress the bone marrow so that there is a diminished output of red cells as well in other words, *anaemias due to these causes are not purely haemolytic*

(b) *Congenital abnormality* of the erythrocytes, e g acholuric familial jaundice sickle cell anaemia

(c) *Unknown factors* as in the acute haemolytic anaemia of Lederer icterus gravis neonatorum anaemia haemolytica neonatorum

B *Splenomegaly* with anaemia as in Banti s disease

4 Red corpuscle oxygen carrying power has been reduced, for example by

Carbon monoxide poisoning
Benzol and nitrobenzene poisoning
Toxaemia—particularly in extensive burns

To supply polymorphonuclear leucocytes, in aplasia of the granulocyte forming portion of the bone marrow

Agranulocytosis

To supply platelets

Essential thrombocytopenic purpura

To supply the substances necessary for coagulation of the blood when this function is disturbed

Haemophilia
Haemorrhagic conditions associated with disordered liver function for example obstructive jaundice
Melaena neonatorum
Erythroblastosis foetalis

To supply antibodies and complement, in certain cases of chronic infections, lowered resistance and non progressive convalescents

To supply serum proteins, in conditions associated with hypoproteinemia

Shock
Malnutrition

To supply formed elements and plasma in conditions associated with lowering of the blood volume—in shock

To Supply Oxygen Carrying Red Corpuscles

When Red Corpuscles have been lost by HAEMORRHAGE

In *surgical* practice severe and sudden haemorrhage is most commonly seen following street accidents more rarely it is encountered as a result of gunshot stabbing or other injuries occasionally it occurs during operation but more often is seen post operatively as a reactionary or secondary haemorrhage following such operations as prostatectomy and tonsillectomy

In the course of *obstetric* practice severe haemorrhage may occur with a placenta praevia with tubal abortion and rupture, or as a post partum complication

In *medical* practice haematemesis from a gastric ulcer or melaena in a case of haemorrhage from a duodenal ulcer are among the commonest causes of severe internal haemorrhage Other causes of haematemesis are cirrhosis of the liver and enlargements of the spleen If the haemorrhage is from the stomach the eroded vessel is usually the splenic vein if from the duodenum the gastro duodenal artery or vein Haemorrhage from the small intestine may occur as a complication of tuberculous dysenteric or typhoid ulceration in the latter as the patient is usually gravely ill at the time the haemorrhage may go unsuspected unless the possibility is constantly borne in mind

Clinical features

It is important for any one practising blood transfusion to be able to distinguish severe haemorrhage from other causes of collapse and be able to give an opinion as to the immediate line of treatment and the optimum moment for surgical intervention should this be a possible eventuality Clearly some one who is in active clinical practice will find this easier than will a pure laboratory worker

General appearance

On approaching a patient who has had a severe haemorrhage one is immediately struck by the deathly pallor of the face and lips. In the same glance it will be noticed that the patient is restless, that he is clamouring for air and that he is constantly asking for water. *Restlessness, air hunger* and *thirst* will distinguish a case of haemorrhage or shock associated with haemorrhage from a case of pure shock. On closer inspection it will be noticed that the skin, for instance of the forehead, is cold and covered with beads of perspiration. The conjunctival mucous membrane is pale and so also are the finger nails.

The mental state, the condition of the pulse, the blood pressure and the tissue turgor vary with the time after the loss of blood that the patient is examined.

The mental condition, apart from some initial giddiness or faintness referable to oxygen lack, is usually normal, that is, except for a fairly natural anxiety, the patient is conscious and rational. If, however, he is seen about two hours after the haemorrhage, he is often confused and irrational, although during this time the circulation has usually improved. The probable explanation is that the initial anaemia has been replaced by a cerebral oedema, a condition which is aggravated by the custom which requires the victim of a severe haemorrhage to be nursed with the head in the most dependant position. The patient's condition is usually relieved by a pillow.

The blood-pressure

At first there is a profound fall in blood pressure. This is due to the sudden removal of a large volume of the circulating fluid which is followed in turn by a diminished venous return, a smaller output from the heart, and hence lowering of the blood pressure. If the patient survives this initial stage, all the forces of physiological compensation will be rallied in an attempt to raise the blood pressure again to a level that will allow oxygenation of the brain and medullary centres to be continued. The effort is initiated by the fall of blood pressure in the carotid sinus and aortic arch which occurs at the same time as the

general fall in blood pressure and as a result of which the tonic inhibitory action of the sino aortic nerves on the vasomotor centre is diminished so that the centre discharges more freely A widespread arteriolar vasoconstriction results which has the effect of reducing the volume of blood supplied to such temporarily inactive areas as the skeletal muscles the skin and intestinal tract This elevation of the peripheral resistance combined with acceleration of the heart results in a rise of blood pressure and increase in blood supply to those areas most urgently requiring it

The compensating rise of blood pressure is commonly to within 15 to 30 mm of the level usual to the individual If the haemorrhage is progressive this relatively high level—about 100 mm —is maintained for some time after the pulse rate has started to rise and until the patient is almost *in extremis*

The important *practical deduction* is that blood pressure estimations are not a reliable indication either of the degree of haemorrhage or as to its arrest or progress

The pulse-rate

The pulse rate is accelerated in all stages of haemorrhage and in a case of moderate severity it will be 110 to 140 to the minute At first the volume is poor—the pulse is thready—but as the blood pressure rises the volume of the pulse improves With further haemorrhage the rate increases usually before the blood pressure shows any sign of falling for the second time

As a result of the haemorrhage the available supply of blood for nourishing the sensitive respiratory and vasomotor centres in the medulla is seriously diminished For life to continue the volume of blood passing through these vital centres must be maintained at the pre haemorrhage level To achieve this the heart accelerates delivering a smaller quantity of blood more frequently

The acceleration is due to reflex stimulation of the cardio accelerator centre through the aortic and sinus nerves This reflex act is initiated by the fall in blood pressure which lowers the tension in the aortic and carotid sinuses

The tissues

(a) Early stages—Dehydration
(b) Late stages—Oedema

With the loss of blood there is a fall of capillary pressure due to incomplete filling of the vascular bed. This disturbs the normal *pressure* balance between blood and tissues in favour of the tissues so that tissue fluids pass into the vessels.

Clinical evidence of this is seen in the dehydrated state of the tissues as shown by the sunken facies and by the great thirst which is such a typical feature. If the blood volume is not restored at this stage by a blood transfusion the reverse process to that just described will ensue. The continued passage of tissue fluids into the circulation results eventually in a dilution of the plasma protein and a disturbance of the osmotic balance between blood and tissues. A condition of hypoproteinemia now exists and fluids begin to pass back again into the tissues. This is aided by the increased permeability of the capillaries which have been damaged by the prolonged anoxaemia. The tissues now become oedematous but usually not to a degree which is demonstrable clinically except at the base of the lungs which if examined at this time will reveal dullness, crepitations and a poor air entry. At *necropsy* in cases of unrelieved severe haemorrhage widespread oedema of the soft tissues, particularly the lungs, is a prominent feature.

The blood

Immediate examination. In attempting to estimate the degree of anaemia little or no help can be obtained from a red cell count or haemoglobin estimation made immediately after a severe haemorrhage. The count at this time is deceptive, as owing to capillary stasis and the discharge of red cells from the spleen it will if anything tend to be raised. This paradoxical phenomenon disappears as the blood volume becomes readjusted by tissue fluid dilution during the subsequent hours (p. 137).

Examination *after twelve to twenty four hours*. Provided there has been no blood or saline infusion or water by mouth or per rectum a blood examination at the end of the first twelve hours will give a comparatively accurate indication of the amount of blood that has been lost. At this time the blood

shows a parallel reduction of haemoglobin and red cells The cells are normocytic and normochromic

Renal changes.

(a) **Blood urea.** The blood urea level is considerably raised during the first thirty six hours following a severe haemorrhage This observation has been made by Wood (1936) of Melbourne who points out the practical value of the investigation as an aid to diagnosis in instances of suspected but unconfirmed cases of concealed haemorrhage Furthermore, there is an added danger in a high blood urea at this time, for a patient already seriously ill from anaemia and drowsy as a result of a high blood urea is not a suitable person to undergo a major operation A preliminary transfusion by improving renal function as well as relieving the anaemia, will give the patient a better chance of recovery

Wood (1936) suggests the following explanation of high blood urea after large haemorrhages

1 When the initial fall of blood pressure occurs the renal excretion immediately diminishes and partial or complete anuria develops, depending on how low the blood pressure has fallen A blood pressure of over 40 mm Hg is necessary to filter fluid from the glomeruli into Bowman's capsule against the osmotic pressure of the plasma proteins
2 As a result of the low haemoglobin and impaired circulation, every organ is inadequately supplied with oxygen This particularly affects the kidneys, where the function of the tubular epithelium is depressed by the anoxaemia It follows that the power of selective reabsorption is impaired and so the blood urea rises
3 A contributory factor appears (in the recovery phase) with the onset of generalized vasoconstriction Should this include the glomerular vessels the renal excreting field is further diminished and the blood urea rises

How much blood can be lost in a single severe haemorrhage without death following? In order to discuss this question it is necessary to have some idea of the normal blood volume This has been estimated by various methods (Congo red method carbon monoxide method) to be between 5,000 and 6,000 c c in

the adult The blood volume is approximately one-eleventh of the body weight so that if the latter is known an approximate figure for the blood volume can be obtained in any given instance

The answer to the question—how much blood can be lost ?—depends essentially upon how rapidly it has been lost A rapid moderate sized haemorrhage is more serious than a greater loss spread over a more prolonged period This is because great as the compensatory powers of the body are they take time to develop Accessory factors influencing the prognosis in any given haemorrhage will be the duration of unrelieved anoxaemia the individual's own physiological powers of accommodation and his state of health The presence of associated disease particularly of the vascular system will further limit the efforts at compensation

Accurate measurements of the blood remaining in circulation after a severe haemorrhage are not easily made For this reason the observations of Keith (1919) made on wounded soldiers during the Great War are of particular interest He found by blood volume estimations that serious symptoms were produced if the haemoglobin fell to below 76 per cent This he regarded as the critical level the level below which the compensatory mechanism could not be relied upon to restore the blood volume unless aided by a transfusion

The lower limit of *rapid exsanguination* compatible with recovery provided a blood transfusion is given is in the region of 50 per cent haemoglobin or half the blood volume Lower levels have been recorded but recovery then is exceptional Below 50 per cent haemoglobin the anoxaemia appears to produce irreversible changes in the tissues Keith's blood volume estimations correspond with the more direct methods of estimation made simply by recovering the blood lost following for example a haematemesis

To summarize one can say in regard to rapid blood loss that

- 400 600 c c (8 12 per cent haemoglobin) is the maximum amount that can be lost without producing any symptoms whatever This is based on our experience with blood donors
- 1 250 1 500 c c (25–30 per cent haemoglobin) is the maximum

that can be lost and recovery occur without transfusion—based upon Keith's work on blood-volume in cases of haemorrhage

2,500–3,000 c c (50–60 per cent haemoglobin) is the maximum amount that can be lost at one haemorrhage without producing death—based upon observations made on large losses into the peritoneal cavity

The Physiology of the Restoration of Blood-volume following Haemorrhage.

The period of restoration of osmotic balance. (*a*) Fluids The restoration of blood-volume takes place in stages

In the case of the blood lost by a transfusion donor (600 c c) the fluid loss is made up in a few hours In the case of a large haemorrhage the fluid loss is usually made up within 24 hours, the rapidity of replacement depending on the ratio of the volume of available tissue fluid to the volume of blood which is lost In each case the tissues provide the fluid—a process which is accelerated if the patient is allowed water to drink, prolonged if water is withheld Fat, plethoric individuals make up their blood volume more quickly than thin people

(*b*) *Solid constituents* These include salts, plasma, proteins, and formed elements *The first solid constituents to be replaced* are the inorganic salts, and they are followed by regeneration of the plasma proteins.

The period of regeneration of the formed elements. It has been pointed out elsewhere that the red blood corpuscles and haemoglobin estimations show little change from the normal immediately after a large haemorrhage, but gradually find their level during the following twenty-four hours as dilution by tissue fluid occurs

The red corpuscles The red corpuscles are restored to normal more rapidly than the haemoglobin, so that the colour index *becomes lower It begins to rise when the red blood corpuscle* count has reached normal According to Whitby and Britton (1937) the red cells are regenerated at the rate of 100,000 cells per c mm a day, so that after a large haemorrhage lowering the red cell count to 2,500,000, theoretically the count will take about three weeks to return to normal if unaided by transfusion.

The early regenerative phase is characterized by the presence of numerous immature red cells. There is a reticulocytosis and possibly some normoblasts. The mature cells are orthochromic and normocytic.

Leucocytes and platelets. There is a rise of platelets during this phase and a leucocytosis up to 30,000 during the first four days after the haemorrhage, which quickly returns to normal.

Haemoglobin. In the case of small losses of blood, as occurs in blood donors involving 400–600 c.c., Brewer (1933) reports that the haemoglobin reduction is from 8–12 per cent., maximal on the fourth day and back at its normal level in 7–14 days.

The stimulus to regenerate haemoglobin in the red marrow is oxygen lack. As the normal level is approached the stimulus of oxygen lack becomes progressively weaker and so the process of regeneration slows down. (Wright, 1918.)

TRANSFUSION DOSAGE IN CASES OF HAEMORRHAGE

The transfusion dosage after haemorrhage will depend upon the quantity of blood lost.

Determination of the quantity of blood lost. The determination of the amount of blood lost may be attempted by:

(i) Clinical estimation.
(ii) Blood volume estimation.
(iii) Haemoglobin estimation.

If the patient is seen within a few hours of the haemorrhage the amount of blood lost can only be assessed from the clinical condition and by estimation of the blood volume. This is because haemoglobin estimations at the time are not reliable.

(i) **Clinical examination.** Loss of blood is a very personal catastrophe and no two individuals suffering a similar loss of blood collapse clinically to the same degree. The extent of associated trauma or disease is naturally a great influence. Sometimes there is visible evidence of the quantity of blood lost — for example in the vomit — but hearsay evidence on this point should be accepted with reservation, for the amount is generally greatly exaggerated (p. 130).

As a rough guide it may be assumed that if the clinical condition is fair, probably not more than one quarter (1,250 c.c.) of the blood volume has been lost; if the symptoms are grave, the

explanatory paragraphs which follow and for the accompanying diagrams

A Haemoglobin estimations are unreliable as *the criterion of the severity of a haemorrhage*

A haemorrhage occurs at the expense of both plasma and corpuscles

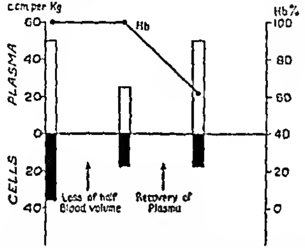

FIG 22 To illustrate how the fall in haemoglobin percentage following haemorrhage is dependent on restoration of plasma volume (Bennett, Dow, Lander and Wright)

In Fig 22 is shown diagrammatically the state of affairs immediately after a severe haemorrhage The left hand column represents the total amount of blood in the normal body This is shown as a vertical column of which the lower two fifths consist of corpuscles and the upper three fifths of plasma If half the blood of the body were suddenly lost we should have the state of affairs shown in the middle column half the corpuscles and half the plasma would have been 'amputated', but the percentage of haemoglobin would be unaltered, remaining at its original figure of, say, 100 per cent

During the next few hours the plasma is restored and the condition seen in the right hand column is produced the volume of corpuscles remains reduced whilst the plasma has returned to normal, and, although the condition of the patient, from the physiological point of view, is probably much better, his haemo

globin has fallen sharply On the other hand, if the plasma volume is more slowly restored—in some cases this takes twenty-four hours or more—a haemoglobin estimation a few hours after the haemorrhage will give an unduly optimistic estimation of the blood loss

From consideration of the diagram it is clear that assessments of severity based on haemoglobin estimations are liable to grave fallacy and that the error is liable to be greatest at moments of extreme importance—that is to say in the hours immediately following a severe haemorrhage It further emerges that the only way of obtaining data of reliability is to employ some method which estimates *the total volume of the blood plasma and the total volume of the blood corpuscles*

B Haemoglobin estimations are unreliable *as evidence of persistent bleeding*

For the same reason namely the slow dilution of the haemoglobin by the tissue fluids, the haemoglobin percentage cannot be accepted as an accurate guide as to whether haemorrhage has ceased or not, for it is clear that in the hours after haemorrhage has begun haemoglobin percentage must be expected to continue to fall whether the actual bleeding has ceased or not Here again observation of the *total blood volume* is the only certain guide available

Fig 23 illustrates this point the three columns on the left show the course of events after a single but rapidly arrested haemorrhage, whilst the three columns on the right show the state of affairs when haemorrhage is continuing simultaneously with the process of dilution There is a steady fall of haemoglobin in both cases The one fact which points inevitably to the conclusion that bleeding is still in progress is that the cell volume has diminished in the second case whereas it remains unchanged in the first

Bennett, Dow, Lander, and Wright (1938) conclude by saying that 'surgical intervention during the acute stages of haematemesis and melaena is almost always carried out on the assumption that bleeding is still in progress There is, we believe, no clinical criterion which gives any firm basis for such an assumption estimation of the blood volume alone gives this important information '

Determination of the quantity of blood to be transfused. After a haemorrhage, as Keynes (1922) has pointed out, there is no need to replace then and there *all* the blood lost. The immediate object of a transfusion should be to restore the blood-volume to the level where the compensatory mechanism for restoration

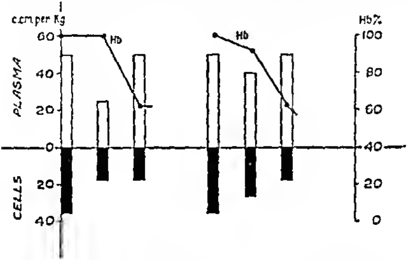

FIG. 23. Diagram showing fall in haemoglobin from dilution of plasma following a single haemorrhage (three columns on left) compared with fall in haemoglobin during continuous haemorrhage (columns on right). Only the estimation of cell volume demonstrates continuation of haemorrhage. (Bennett, Dow, Lauder and Wright.)

of blood volume can become effective. Keith (1919) has shown that this is in the neighbourhood of 75 per cent. haemoglobin.

If the signs of haemorrhage are marked a transfusion of 750 c.c.–1,500 c.c. will be required to restore the blood volume to this level. Two donors of a suitable group should be obtained as soon as possible. Later during early convalescence one's ultimate object of restoring the blood to its prehaemorrhage level can be attained by iron and dieting, and if necessary by a further transfusion.

The place of transfusion in the treatment of gastric and duodenal haemorrhage.

It would serve no useful purpose at this stage to enter deeply into so controversial a subject as the treatment of gastro-duo

denal haemorrhage but since the issue cannot be altogether avoided some attempt will be made to define the position of transfusion in relation to internal haemorrhage

An important difference between the intestinal haemorrhages and those due to most accidents or surgical operations lies in the question of *access* to the bleeding point In haemorrhage of intestinal origin ligation of the bleeding vessel is a *hazardous proceeding* whereas *in haemorrhage of traumatic origin the bleeding point is usually relatively easy of access and control* In other words when the question of transfusion arises the bleeding point in the one case has been secured and in the other it has not

For this reason in cases of gastro duodenal haemorrhage the tendency has been to adopt a more conservative line of treatment than with haemorrhage of traumatic origin The particular circumstances will decide the policy to pursue Briefly the possible methods of treatment in relation to blood transfusion are

1 A large volume *transfusion given at a drip rate* till the haemoglobin is in the neighbourhood of 75 per cent (not 100 per cent —p 114) and then either

(*a*) Conservative treatment without operation or

(*b*) Operation

2 A small volume blood transfusion to relieve the more distressing symptoms due to oxygen lack and to promote haemostasis followed by the régime outlined below

In such a case it will not be justifiable to operate without further raising the haemoglobin level

3 No blood transfusion and a policy of non intervention This consists of enforced rest by morphine restoration of blood volume by rectal or intravenous fluid starvation by the mouth or alternatively the Meulengracht régime

The importance of adequate transfusion in cases of gastro duodenal haemorrhage

The tendency in transfusing acute anaemias is to give only enough blood—usually 500 c c —to combat the existing haemorrhagic shock The immediate effect of such a transfusion is so dramatic that a further transfusion to restore the haemoglobin

to within limits where regeneration can become effective is not considered and it is decided to leave well alone In reality a patient at this stage is sitting on the top of a volcano for there is no reserve should another haemorrhage ensue

This attitude of mind is encouraged by the fear that a further or larger transfusion by increasing the blood volume is likely to raise the blood pressure and so restart the haemorrhage This opinion is based on experiences gained with the more rapid short transfusions which were used before the slower drip technique had been introduced It is also based upon a physiological misconception In health the blood volume is remarkably constant and after a considerable haemorrhage even if no transfusion is given it is restored to normal by the tissue fluids within a few hours In other words, a drip transfusion is restoring rather than distorting the physiological balance—a change which the organism would otherwise have to attempt on its own—and perhaps fail in the effort

If the blood is introduced at a drip rate it has been my experience that recurrence of haemorrhage is a great rarity—certainly it is not more frequent than the recurrence of haemorrhage in those cases from which transfusion is withheld

In conclusion one can assert that the advantages of raising the haemoglobin adequately (though not back to the normal) particularly in cases of haemorrhage from peptic ulcer outweigh by far the disadvantages By supplying fibrinogen a firmer clot is likely to be formed and by restoring or partly restoring the corpuscular content the patient is not only put in the way of a more rapid recovery but is better prepared for an operation should this be decided upon or to withstand another large haemorrhage should this supervene

The place of operation in the treatment of gastro-duodenal haemorrhage

A discussion on the place of operation is almost outside the scope of this book yet some mention of it must be made as it is so closely linked with the question of blood transfusion

Operation for relief of gastric or duodenal haemorrhage may be performed as an emergency measure shortly after the haemorrhage or as a prophylactic measure in an interval

period We are here concerned only with the problem of immediate operation Such an operation on a person who is dangerously ill can only be justified if it is being performed to arrest haemorrhage when all other attempts have been unsuccessful These circumstances *do* occasionally arise, and when they do operation by an experienced surgeon with a drip blood transfusion maintained throughout is likely to be life saving Before embarking on such an operation, there should be reasonably reliable evidence of

(a) A chronic ulcer—in the form of existing recent X rays or a long standing dyspeptic history
(*b*) Persistent haemorrhage—most accurately shown by a blood-volume estimation

In many patients the origin of the haemorrhage will be uncertain, and I have myself on several occasions made a necropsy on a case of haematemesis in which the stomach was full of blood, but no demonstrable source could be found In such cases, and they can rarely be excluded with certainty, transfusion offers the best hope of immediate relief Operation at a later date to prevent recurrence of haemorrhage and after the patient has returned from convalescence is quite a different matter, and we are not concerned with it

The Rate of Introduction

The rate will depend upon whether the bleeding point has been secured or not

If the bleeding vessel or vessels have been secured or controlled, as, for example, will usually be possible after an accident involving the limbs, after post partum haemorrhage, or a post-operative haemorrhage, a relatively rapid transfusion should be given as soon as possible, for in these cases there is an urgent need for red cells to maintain oxygenation of vital centres Fortunately also, these haemorrhages usually take place in healthy people—in other words in individuals with an undamaged myocardium In these circumstances a rapid transfusion is safe because the total blood-volume has been diminished by the haemorrhage

It is my opinion *that acute anaemia due to sudden severe haemorrhage is the* **only indication** *for what may be termed the*

old fashioned rapid *blood transfusion and even then only if the bleeding vessel has been secured*

If a total dose of 1 500 c c is contemplated not more than 600 c c should be given by a rapid method The remaining 900 c c should be run in at the usual drip rate of 40 drops a minute

If the bleeding point cannot be secured as is likely to be the case if the haemorrhage arises from for example a bleeding peptic or typhoid ulcer the rate of introduction will necessarily have to be slow

The exact rate will depend upon whether the haemorrhage has stopped or is still progressing All cases should be treated by the continuous drip method and the rate controlled by repeated haemoglobin estimations

In cases in which exsanguination is extreme it may on rare occasions be advisable to run in the first 400 500 c c relatively rapidly to relieve the anoxaemia and the risk be taken of restarting the haemorrhage from the open vessel Such action is only justifiable if it seems quite certain that if the blood were introduced slowly the patient would not recover

HAEMORRHAGE AFTER TONSILLECTOMY

I am indebted to J R Peacock of St George s Hospital London for the substance of the account which follows

Haemorrhage after tonsillectomy is either reactionary that is to say occurring during the few hours immediately following the operation or secondary occurring on from the eighth to the twelfth day

Diagnosis

In the case of reactionary haemorrhage diagnosis is seldom difficult in that visible haemorrhage usually occurs Occasionally however this may appear to be very slight in amount particularly if the patient has for some time been swallowing the blood It is because of this possibility that all specimens of vomit containing blood should be *preserved* by the nursing staff

In addition in all these cases a close watch should be kept on the pulse colour, breathing and skin temperature

As soon as bleeding of any kind occurs, an immediate inspection of the throat is necessary The clot in the tonsillar fossa, which is nearly always present should be removed, and a diagnosis made as to whether the bleeding is coming from a spurting vessel or from a generalized ooze

In Children

In children, in whom bleeding is occurring following tonsillectomy, the differentiation between arterial bleeding and a general ooze is not always easily made, as the patient's co operation is to some extent necessary and that is often difficult to obtain In my opinion, in all cases of doubt, these small patients should be returned immediately to the theatre, an anaesthetic administered and the bleeding point found and ligatured

An additional reason for adopting this policy at an early stage in children is the fact that their general condition can more suddenly and dramatically change for the worse than is the case with adults The child should in every case be blood grouped before being returned to the theatre

In Adults

Arterial bleeding

In adults, in those cases where a spurting vessel is seen, the procedure is the same, the patient is returned to the theatre, and the vessel tied The blood group is determined at the earliest possible moment serum is collected for cross matching, and a donor warned in case a transfusion is necessary

General ooze.

Where a general ooze is thought to be the causative factor, the clot may be removed, and where the patient permits, pressure applied to the tonsillar fossa simultaneously from the inside and without, with wool moistened in 1/1000 adrenaline The application of Stypven Russell viper venom to the bleeding area can be of value, and an intramuscular injection of 20 to 40 c c of Sangostop is non toxic and worthy of trial Thereafter the patient is given morphine, grain one quarter, and ice is applied to the neck, a careful watch being kept on the pulse rate, colour, skin temperature, and respiration

Blood grouping should be determined at this time, and serum

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obtained for cross matching, so that last minute disturbances may be avoided (see Fig 12, p 42)

If the haemorrhage should persist, it must rest with the medical attendant's judgement and his observation of the points mentioned above as to whether and when the patient should be returned to the theatre, but in my experience this should be done in all cases of persistent haemorrhage at or before the time when lowering of skin temperature becomes appreciable in the patient's forehead

Where surgical measures become necessary, every possible attempt should be made to avoid suturing the pillars of the fauces together, as although this procedure may be immediately effective the resultant scarring of the posterior pillars removes the guard to the nasopharynx and predisposes the patient to subsequent nasopharyngeal catarrh, and even to eustachian deafness

Blood Transfusion

The part played by blood transfusion in these cases can be of the utmost importance In very severe cases, where, for some reason surgical intervention has been delayed, a transfusion may be necessary at the time the patient is returned to the operating theatre More commonly, it is desirable that the haemorrhage should first be arrested, and a transfusion administered to replace the blood which the patient has lost In still more difficult cases where the patient's general condition when first seen does not permit the administration of a further anaesthetic, it may be necessary to transfuse, in the hope, as sometimes occurs, that the transfusion will induce the cessation of haemorrhage or that a sufficient improvement in the patient's general condition will be obtained to allow of the required anaesthesia being given

Prophylactic measures.

In any consideration of haemorrhage following removal of tonsils, two preoperative points should be born in mind

In the case of a patient giving a history of unusually prolonged bleeding in the past, the pre-operative administration of intravenous calcium should be undertaken over a period of from three to four days, although in the average patient this precaution is unnecessary.

after maintaining this level by repeated small transfusions at short intervals The advantages of this method are threefold hospitalization is reduced to a minimum for after the initial transfusion it will as a rule only be necessary to admit the patient for observation for one day on the occasion of each retransfusion wide excursions in the haemoglobin and red cell content of the blood are avoided and so a minimum of strain is placed upon the bone marrow By starting the treatment with a continuous drip transfusion the total number of transfusions required is reduced which is a more rapid and less tedious way of producing the optimum blood picture

Large volume transfusion in stages If the initial elevation of the haemoglobin is calculated to exceed 1 500 c c s of blood the transfusion should be given in two or more stages with an interval of three days between each transfusion

Frequency of transfusion Following the initial large volume blood transfusion the frequency of subsequent small transfusions will depend upon the rate of fall of the haemoglobin level as determined by regular haemoglobin estimations Most patients will require transfusions of approximately 700 c c at weekly or fortnightly intervals although in some instances a longer period will be possible

Optimum haemoglobin level to be maintained Curiously enough a haemoglobin percentage within the limits of normality does not always suit these patients as well as lower levels The optimum for each individual can only be determined by trial In Hurst s case reported by Harrison (1931) and Kark (1937) the patient felt most comfortable when his haemoglobin was between 60 and 70 per cent whereas at a higher figure he was not so well Imrie (1935) reports a case in which the optimum level was in the neighbourhood of 50 per cent

The expectation of life In Hurst s case mentioned above the patient received at least 290 transfusions spread over 9 years during which he led an active and full life In another case of Hurst s reported by Kark (1937) the patient had some 61 transfusions in 7 years and in a third case under this physician and reported by Knott (1934) the patient was maintained in good health for 16 months by 53 transfusions In a case of my own a useful life was prolonged for a year by 27 transfusions

Complications The recipient of repeated blood transfusions is more likely to develop a reaction than the recipient of a single transfusion but the risks run can be reduced to a minimum by careful cross matching before each transfusion and by *introducing the blood at a drip rate* In spite of these precautions reactions in the form of rigors or attacks of urticaria will occur from time to time in these multiple transfusion cases

Another sequel of frequent transfusion is that the patient may develop haemochromatosis This was present in Harrison and Kark s case which had 290 transfusions It is characterized by a slate coloured complexion pigmented conjunctivae and teeth a dry, hairless skin and a large tender liver Haemochromatosis is a storage disease and is presumably due in these cases to an inability to deal with the excess of iron introduced by the transfusions

The transfusion of polycythaemic blood to cases of aplastic anaemia The use of polycythaemic blood for transfusion purposes has been practised for many years Although perhaps this is not quite such an unpleasant practice as the transfusion of leukaemic blood to agranulocytic patients it should be reserved as far as possible for incurable cases and aplastic anaemia can probably be included in this group Polycythaemic blood is very thick and does not always run well from the donor and for the same reason it is not very satisfactory blood to introduce into a recipient by a gravity method unless it has been previously diluted with saline

Secondary or symptomatic aplastic anaemia In cases of secondary aplastic anaemia the cause must first be removed They are then likely to respond very well to the transfusion of blood carried out as outlined above

PERNICIOUS ANAEMIA

As is well known pernicious anaemia is due to the absence from the gastric juice of a ferment-like substance called the intrinsic factor Normally the intrinsic factor of the stomach acts upon an extrinsic factor contained in the diet to produce the haemopoietic principle which is absorbed from the intestine and which is essential for the proper development of bone marrow megoblasts into erythroblasts and normoblasts Until

after maintaining this level by repeated small transfusions at short intervals. The advantages of this method are threefold: hospitalization is reduced to a minimum, for after the initial transfusion it will as a rule only be necessary to admit the patient for observation for one day on the occasion of each retransfusion; wide excursions in the haemoglobin and red cell content of the blood are avoided and so a minimum of strain is placed upon the bone marrow; by starting the treatment with a continuous drip transfusion the total number of transfusions required is reduced, which is a more rapid and less tedious way of producing the optimum blood picture.

Large volume transfusion in stages. If the initial elevation of the haemoglobin is calculated to exceed 1 500 c c s of blood the transfusion should be given in two or more stages with an interval of three days between each transfusion.

Frequency of transfusion. Following the initial large volume blood transfusion the frequency of subsequent small transfusions will depend upon the rate of fall of the haemoglobin level as determined by regular haemoglobin estimations. Most patients will require transfusions of approximately 500 c c at weekly or fortnightly intervals, although in some instances a longer period will be possible.

Optimum haemoglobin level to be maintained. Curiously enough a haemoglobin percentage within the limits of normality does not always suit these patients as well as lower levels. The optimum for each individual can only be determined by trial. In Hurst's case reported by Harrison (1931) and Kark (1937) the patient felt most comfortable when his haemoglobin was between 50 and 70 per cent, whereas at a higher figure he was not so well. Imrie (1935) reports a case in which the optimum level was in the neighbourhood of 50 per cent.

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it became known that the haemopoietic principle was contained in liver and so could be supplied in the diet these patients lived by blood transfusion To-day blood transfusion is the exception rather than the rule

Indications for blood transfusion

General principles For most patients however anaemic the standard liver therapy is the safest and best method of treatment

We must not forget that blood transfusion is an operation associated with a definite mortality and that pernicious anaemia patients with the possible exception of patients with severe sepsis are the worst possible subjects for blood transfusion on account of the poor state of their myocardial muscle

Because of this there is always the danger of circulatory failure from overloading from speed shock or as the result of a rigor so that it will generally be safer to persist with liver therapy unless there is a very good reason for giving blood (See contra indications)

Indications It is probable though not inevitable that transfusion will be necessary in the following circumstances

(i) If the *red cell count is ous less than* 600 000 red corpuscles per c mm when the patient is first seen In such a case the patient should receive a transfusion of 600 c c of carefully cross matched citrated blood of the same group given at a drip rate together with an intravenous injection of liver extract No blood transfusion at all is infinitely to be preferred to a rapid transfusion at this stage

(ii) *Failed reticulocyte response to liver therapy* If the reticulocyte response to liver therapy is good there is seldom further cause for anxiety but if this is unsatisfactory a blood transfusion may induce a reticulocytosis by stimulating the bone marrow

(iii) *Severe clinical condition* No improvement from liver therapy even by parenteral injection can be expected before the fourth day If the clinical condition of the patient suggests that she may die within this period an initial blood transfusion should certainly be given

(iv) *Presence of complications* Apart from the anaemia itself the indications for blood transfusion in pernicious anaemia will

include such complications as gross sepsis, acute appendicitis, pregnancy, and trauma.

Special considerations. *Reactions.* It has been emphasized that patients with pernicious anaemia are particularly liable to reactions following blood transfusion. Many of them tolerate the initial increase in blood-volume without incident, but should a rigor be superimposed, the anaemic myocardium may not be able to withstand the mechanical strain of the upheaval. It is therefore of particular importance to avoid such a disturbance, and to this end all these patients, without exception, should receive the blood at a *drip rate*, and from a donor of the same blood group.

Pseudo-agglutination may cause confusion in these cases, so that it is of importance that some one with experience, preferably of the naked-eye method of interpretation, should be available for consultation over the direct test.

The *volume* of blood to be transfused will depend on the haemoglobin level at the time.

Macrocytic anaemia of pregnancy.

Definition. The macrocytic anaemia of pregnancy, at one time called the haemolytic anaemia of pregnancy, but renamed because haemolysis is not a feature of the disease, appears to be a form of pernicious anaemia induced by pregnancy and relieved by administration of haemopoietic principle.

Indications for blood transfusion. In those instances in which the anaemia is particularly grave or the response to liver therapy is slow, one or more transfusions may be required to prepare the patient for the extra demands necessarily to be expected during labour. No patient should be allowed to go into labour without a transfusion if the haemoglobin is below 40 per cent. If the child is to be delivered by Caesarean section, a transfusion should be given three days before delivery and another after the operation. There is no increased tendency to post-partum haemorrhage.

Precautions. The same care must be taken in the selection of cases for transfusion as in pernicious anaemia, and the transfusion must be given slowly, using cross-matched donors of the same blood group only.

WHEN RED CORPUSCLES HAVE BEEN DESTROYED BY HAEMOLYSIS

Transfusion in the hæmolytic anaemias, with special reference to Acholuric familial jaundice and Lederer's anaemia

In a few isolated instances transfusion to patients with haemolytic anaemia has been associated with a severe hæmolytic reaction (Dawson 1931) For this reason there has grown up a tendency to avoid transfusion in these cases as it is said to be dangerous Actually the number of severe reactions appears to be no greater than following transfusion to any other severe anaemia so there seems to be no reason to advise its discontinuance

The precautions taken will be the same as when transfusing any severe anaemia—namely the use of a donor of the same group careful cross matching and introduction of the blood at a drip rate

ACHOLURIC FAMILIAL JAUNDICE

In acholuric familial jaundice a transfusion of blood is usually followed by a marked improvement in the patient's general condition and as a pre operative measure—before splenectomy—it should rarely be omitted

Vaughan (1938) has had experience of blood transfusion to ten different patients with acholuric familial jaundice There was a mild reaction in one of this series only and she regards it as a very valuable therapeutic remedy

Kremer and Mason (1936) strongly advise transfusion and say that treatment with liver and other haemopoietic substances is associated with a deterioration in the general condition of the patient They emphasize that the transfusion should be given at a slow drip rate In two of their cases an initial relatively rapid transfusion was given but this resulted in such a severe rigor and in increase in haemolysis with jaundice in one of the cases that it was decided to use the drip technique when retransfusion became necessary later This was accomplished in each instance without the ill effects previously observed

LEDERER'S ANAEMIA

In Lederer's anaemia transfusion is generally regarded as a specific. The theory is that an anti haemolytic agent is introduced with the transfused blood and is responsible for the arrest of the haemolytic process. It is true that Payne (1934) has recorded a fatality, in spite of correct grouping, in this anaemia but against this can be set amongst others the successful cases of Greenwald (1938) and of Joules and Masterman (1935) who conclude that 'it is unjustifiable to delay treatment by transfusion'. The rapid improvement from being gravely ill is generally most striking.

Precautions Blood transfusion is not contra indicated in the haemolytic anaemias, in fact at present it may be said to hold out the only hope of cure in certain types. As in any severe anaemia however it is necessary that extra precautions should be taken to avoid a reaction. To this end it is essential that the transfusion be given at a drip rate, that a donor of the corresponding blood group be employed and that the direct test be carefully carried out.

Considerable publicity has been given to a few isolated reports of reactions, but this should not be allowed to influence our faith in the good results which generally follow blood transfusion to these patients.

WHEN THE RED CELL OXYGEN CARRYING POWER HAS BEEN REDUCED

In carbon monoxide poisoning

In coal gas poisoning a considerable proportion of the circulating haemoglobin is converted into carboxyhaemoglobin and so rendered useless for oxygen carrying purposes. Blood transfusion may in these cases be of value by supplying healthy red corpuscles with full oxygen carrying power which can maintain the necessary processes of tissue oxygenation. For replacement transfusion see p. 154.

In benzol poisoning

In poisoning with benzol the circulating oxyhaemoglobin is converted into methaemoglobin. A blood transfusion will

help by providing normal red corpuscles of normal oxygen carrying capacity

In toxaemic states—Severe Burns diphtheria

In toxic states there may be both a qualitative and a quantitative reduction of the oxygen carrying power of the blood That is red corpuscles may be reduced in number as a result of destruction for example, by a haemolytic toxin or *more commonly* from depression of the regenerative centres in the bone marrow Alternatively, the corpuscular efficiency may be reduced owing to the prolonged action of the toxin upon the contained haemoglobin

In such circumstances a transfusion of healthy blood may succeed in breaking the vicious circle present

Burns In patients with early severe burns transfusion serves a double purpose it restores the blood volume which by loss of fluid into blisters or dressings may be enormously depleted and it supplies serum proteins which not only enable the osmotic balance to be maintained but have a very important nutritive value

Exsanguination transfusion

By exsanguination transfusion is meant the preliminary withdrawal of a quantity of blood—followed by transfusion

The rationale of this procedure is open to doubt The intention is to remove in cases of profound toxaemia and septicaemia as much toxic blood as possible and to replace this with non toxic blood having a normal or greater than normal content of immune bodies fresh complement and healthy leucocytes and red cells As Powers (1938) points out, the removal by exsanguination of sufficient toxins or bacteria to be beneficial seems doubtful since toxins and bacteria do not arise in the blood but rather in a septic focus A more reasonable procedure is to try to stimulate the body to eliminate its own toxins by the intravenous administration of glucose and saline and to supply complement and anti bacterial substances by ordinary transfusion

If exsanguination transfusion is to be carried out the amount of blood withdrawn at one time should not be more than 800 c c , as greater amounts may be accompanied by fainting

Repeated venesection followed by transfusion with the object of completely replacing the damaged corpuscles has been suggested, but unfortunately in toxaemic states the trouble does not lie only with the blood: the tissues themselves have frequently been damaged beyond repair, and the complete replacement of the circulating blood could not be expected to achieve very much in such circumstances.

To Supply Polymorphonuclear Leucocytes

AGRANULOCYTOSIS

In agranulocytosis there is an intense neutropenia, secondary to pyramidon or other such drug poisons Blood transfusion can only relieve these cases by supplying the recipient with leucocytes which in turn are converted into nucleotide

There are several ways of supplying leucocytes to the agranulocytic patient·

1. **Ordinary blood transfusion.** Some authorities, notably Jackson, Parker, and Taylor (1932), found that blood transfusions actually did more harm than good, though Whitby and Britton (1937) say that they have had the opposite experience The disease is not common enough or the list of published cases great enough to enable me to express a definite opinion either way.

2. **Transfusion of 'leucocyte cream'.** The transfusion of leucocytes only has been suggested by Strumia (1934) If citrated blood is allowed to stand, it settles into three layers—a superficial layer of plasma, an intermediate or buffy coat of leucocytes, and a lower layer of red cells Separation of the leucocytes is made easier by standing the blood in a long narrow-necked bottle.

3. **Transfusion of blood with a high leucocyte count.** Theoretically, preliminary injection of nuclein to a donor will, by raising his leucocyte count, render his blood more suitable for transfusion to patients with a neutropenia (p. 159).

4. **The transfusion of leukaemic blood.** There is some difference of opinion on the desirability of transfusing the blood of a patient with myeloid leukaemia to an agranulocytic. Those who are opposed to the practice say that they do not see why, because a person has one disease, he should be given another.

They point out that leukaemia may be due to a virus infection and for that reason it may be transmissible Spontaneous leukaemia in animals as Watts (1938) has pointed out can be transferred to other animals of the same species even by inoculation of a few cells *Whole or citrated blood* The results obtained by the use of whole and citrated blood are similar

The protagonists of the transfusion of leukaemic blood (Degelmann 1937) refer to cures obtained by this method of transfusion and justify the procedure on these grounds They point out that a transfusion of 500 c c of leukaemic blood is equivalent in leucocytic value to 20 litres of normal blood

To Supply Platelets

ESSENTIAL THROMBOCYTOPENIC PURPURA

Essential thrombocytopenic purpura is a disease associated with a quantitative deficiency of platelets This deficiency can be made up by transfusions Tocantins (1936) claims to have cured 46 per cent by repeated transfusion alone that is to say without splenectomy and it can almost always be relied upon to control a severe haemorrhage Certainly transfusion should be given a reasonable trial before splenectomy is considered

Amount and frequency of transfusion It has been found that bleeding in purpura haemorrhagica does not usually occur until the platelets fall to a level of 40 000 per c mm or less This is the so called critical level The object of a transfusion is to restore the platelet count above this critical level It will be remembered that the platelet count in the normal individual is between 250 000 and 500 000 per c mm A transfusion of 500 c c will therefore supply approximately 50 000 platelets per c mm In 3–5 days the transfused platelets are apparently destroyed they certainly disappear from the circulating blood for the platelet count falls to its pre transfusion level In the meantime however the haemorrhage has been arrested and may not recur for weeks or even years In a few cases multiple transfusions may be required to produce the desired effect

Transfusion and splenectomy

In those cases in which splenectomy is decided upon a transfusion should always be given preferably before rather than

during the operation Whenever possible transfusion should be avoided during anaesthesia or any form of unconsciousness, as in these circumstances incompatible reactions may go undetected

Transfusion of platelets only. A method of separating platelets only for transfusion has been described by Tonio (1936) This is of questionable value since in most cases of purpura haemorrhagica there is some degree of anaemia from haemorrhage and a transfusion has the advantage that it restores the red corpuscles as well as the platelets

To supply Antibodies Phagocytes, and Complement

Transfusion in the presence of sepsis and infective states.

Septicaemia Blood transfusion can be of the greatest help in the attack on local and general infections particularly if it is used early in the course of the disease and not as a last resort

The new blood brings in not only healthy red cells and leucocytes, but also fresh complement and antibodies

The management. The management of these transfusions requires extra care, for these patients are even more liable to reactions than are cases of severe anaemia

My own experiences have led me to the following conclusions

1 The blood should be introduced at a *drip rate*
2 *Repeated* transfusions at *short* intervals and of *small* volume produce the best results
3 Citrated and uncitrated blood produce the same results
4 Immuno transfusion, &c

In considering the transfusion of blood to septic cases two points of special interest arise The first of these is the consideration of the claims made for the use of unaltered blood, and the second concerns the attempts that may be made to raise the bactericidal quality of the donor's blood

Citrated or uncitrated blood? There are those who believe that sodium citrate damages the leucocytes and who therefore prefer to use whole blood or defibrinated blood In practice the contention is a questionable one, although it must be

allowed that citrate cannot at any rate improve the quality of the leucocytes which play such an important part in transfusion for sepsis

Defibrinated blood transfusion The use of defibrinated blood for transfusion was first practised by Bischoff in 1835 Following the discovery of blood groups in 1901 and up to the time that sodium citrate appeared (1915) it was the most commonly practised method of transfusion

Defibrination of the blood has the advantage that the phagocytic power of the leucocytes is undisturbed and it is for this reason that defibrinated blood is preferred to citrated blood by some when transfusing septic cases

The method of defibrination The main points in the method of collection of defibrinated blood are as follows

1 No anticoagulant is added
2 A twisted glass rod is inserted through the cork of the collecting flask to form a medium upon which the fibrin can be deposited and afterwards removed
3 While the blood is flowing the collecting bottle is fairly vigorously agitated by a rotatory movement—without going so far as to shake the blood This agitation should be maintained for a full ten minutes after collection is completed
4 The twisted glass rod with the deposit of fibrin attached is removed

Approximately 10–20 c c of clot forms for every 500 c c of blood

The blood may now be introduced by any method familiar to the operator

Discussed elsewhere

1 The use of defibrinated blood where no anticoagulant is available

2 The use of defibrinated blood in the treatment of bleeding cases

Methods of raising the bactericidal power of the donor's blood

In an attempt to raise the bactericidal power of the donor's blood for transfusion to septic or infected cases two methods

of treating the donor are available In the one method an attempt is made to produce a leucocytosis, and in the other the object is to raise the antibody content of the serum—the so-called immuno-transfusion

Method of inducing leucocytosis in the donor.

Nuclein 2–3 c c (10 per cent nucleic acid, Parke Davis & Co), is injected intramuscularly into the donor In a healthy person this gives a 100 per cent rise of leucocytes in two hours, and this rise is maintained for about two hours or more (MacLean, 1938) The increase in the white cells is mostly in the polymorphonuclears As regards the quality of the leucocytes, MacLean found that in bactericidal tests they were of exactly the same efficiency as those present in the blood-stream Therefore, the bactericidal power of the blood was enhanced in the same proportion as the increase of polymorphonuclears In 100 cases there was no local or general reaction in the donor

The value of this method of preparing the donor can only be decided by the clinical results obtained, and so far no series of this kind has been reported It would also be of interest to make white cell counts before and after transfusion to determine whether there was a true quantitative increase of polymorphonuclears in the recipient

IMMUNO-TRANSFUSION

Definition.

By an immuno-transfusion is meant the transfusion of blood from a donor who has been immunized against an organism either by an injection of vaccine or as a result of having recently suffered from the disease. There are three main types of immuno transfusion

Non-Specific. (*a*) From the self-immunized donor—e g a patient convalescent from typhoid, poliomyelitis, carbuncle, osteomyelitis.

Specific. (*b*) From a donor immunized against an autogenous vaccine.

Non-Specific. (*c*) From a donor immunized against a stock vaccine.

Principles involved—the theory of immuno-transfusion

It was originally suggested that by raising the antibody content of the donor's blood particularly if the antibodies were specific that the value of the blood transfused would be enhanced proportionately. In practice unfortunately this theoretically excellent proposition is only occasionally confirmed.

To some extent the inconsistent and disappointing results of immuno transfusion can be explained when we consider certain misconceptions which have arisen in connexion with the rationale of the procedure.

In the beginning the justification of immuno transfusion was largely based upon observations made by Wright, Colebrook, and Storer (1923) upon individuals affected by staphylococcal infection in whom they found the bactericidal power of the blood to be diminished both in regard to the phagocytic power of the leucocytes and the antibody content of the serum. Immuno transfusion seemed to be the solution for these cases. This state of affairs however as pointed out by Hare (1935) does not apply to individuals affected by haemolytic streptococci in whom the bactericidal power of the serum is in fact raised above normal.

In these patients

> it was shown that although the phagocytic power of the leucocytes suspended in normal serum was indeed below normal the serum of these patients contained bacteriotropins or heat stable opsonins which were able to compensate for the deficiencies of the leucocytes so that the defibrinated whole blood of these acutely infected patients was in almost every case tested much more actively phagocytic for haemolytic streptococci than normal (Hare 1935)

The practical importance of this observation is considerable for it explains the failure of immuno transfusion in so many of the cases in which it has been tried. The failure is due to the fact that the patient already has a high degree of immunity—much higher than the donor—to his own infection.

It also explains or suggests the reason for the success of immuno transfusion when this occurs. The immunized donor develops a leucocytosis as well as immune bodies and it is possible that it is this fraction of the blood that is of value to

patients whose leucocytes are subnormal in phagocytic power, even though increased in number

This explanation gains additional support from the fact that the results obtained by non specific immunization of donors, with a stock vaccine, are frequently as good and in the opinion of some, better than the results from specifically immunized donors

Specific or non-specific immunization?

Several points in favour of non specific immunization have already been mentioned It seems from Hare's work that a patient with a severe infection has as a rule a high concentration of antibodies in the serum, bactericidal to his own particular infecting organisms For this reason what Wright (1919) said twenty years ago about the use of vaccines can well be applied to immuno transfusion to day

'We should discard the confident dogmatic belief that immunisation should be strictly specific We should instead proceed upon the principle that the best vaccine to employ would always be the vaccine which gives on trial the best immunising response against the microbe we propose to combat

In practice the results obtained by using a stock vaccine upon a donor are, in fact at least as successful as when an autogenous vaccine is made, nor does the use of a stock vaccine involve the delay or require the technical help of a bacteriologist in its preparation

It may happen in rare cases that the bactericidal power of the patient's serum is below normal and in these cases specific immunization may be the method of choice

Preference for non-specific immunization

Quite apart from the relative merits of the different methods of immuno transfusion the time factor will more often than not decide the point as to which is to be used Obviously a patient who is gravely ill cannot wait for three weeks while the donor is being immunized from an autogenous vaccine In fact there may not be time even to await the result of a blood culture In the gravely ill, therefore, a rapid method of immunization must be employed

Preference for specific immunization

In a chronic long standing illness there will be time to prepare an autogenous vaccine and to immunize a donor with it Specific immunization is perhaps most strongly indicated when there is evidence that the bactericidal power of the recipient s serum is below normal

In some cases the rapid course of the disease makes it impossible to obtain a culture prepare a vaccine and immunize one or more donors In such cases a culture should be obtained as early as possible and the patient transfused in the ordinary way until the immune blood is ready

Method of preparation of the donor for immuno-transfusion

Non-specific immunization There are two main methods (a) using a stock staphylococcal vaccine (b) using dead typhoid bacilli

(a) *Stock vaccine* The donor is given a single dose of 1 000 million mixed staphylococcal vaccine into the left deltoid region five hours before the intended transfusion The injection is preferably made intramuscularly but may be subcutaneous The donor may return to work after his injection to report in five hours time for blood letting This method inconveniences the donor very little As a rule he does not feel any ill effects although the arm may get a little stiff and sore in the shoulder region just as it does after typhoid inoculation The method also has the advantage that the donor need only be away from his work on two occasions both on the same day

(b) *With dead typhoid bacilli* Crocker (*et al*) (1935) found that the opsonins in the donor's blood are increased from five to ten times eight hours after the intravenous injection of 50 million dead typhoid bacilli Their method of treating the donor is as follows The donor is put to bed and given 50 million killed typhoid bacilli intravenously Within an hour there are symptoms of headache and malaise with chill and fever the temperature rising to the region of 104° F A further 25 million is given intravenously within the next hour At the end of eight hours and at the height of the fever the donor s blood is

drawn for the transfusion The donor's condition returns to normal in twenty four hours

Specific immunization For the most part the dosage here will be smaller and spread over a longer period of time The exact dosage will clearly depend upon the virulence of the organisms concerned

To immunize a donor against infective endocarditis it will probably be safe to give three doses of vaccine of *Streptococcus viridans* at weekly intervals starting with 20 million and increasing to 40 million and then 60 million

To immunize a donor against typhoid an initial dose of 250 million will be safe followed by 500 million and 1 000 million at weekly intervals

SUMMARY

After a successful immuno transfusion it is difficult to be certain that the improvement is due to the immuno bodies introduced rather than to the transfused blood *per se*

Immuno transfusion originated in this country in 1919 with the work of Wright and it has been given an extended trial here during the last twenty years The peak of its popularity is now well passed The method reached the continent of Europe some years after it had been advocated in London and is still being extensively used particularly in France The feeling at the present time in Britain is that immuno transfusion should only be tried after ordinary transfusion has failed

A new factor which has greatly reduced the number of indications for this method of transfusion has been the advance in chemotherapy due to the advent of the sulphonamide group of drugs

To supply the Substances necessary for the Coagulation of the Blood

HAEMOPHILIA

It is necessary to know something of the aetiology of haemophilia in order to understand how a blood transfusion brings about its beneficial effect

Haemophilia is a disease confined to men but transmitted

by women It is associated with a prolonged coagulation time but normal bleeding time It appears to be due to a deficiency affecting the organic clotting complex and not to the calcium content of the blood which is normal It has been suggested that the platelets are abnormally resistant and so do not disintegrate and liberate the thrombokinase when bleeding occurs This is supported by the observation that they have been found intact in shed blood long after the haemorrhage has stopped Others believe that the platelets are not responsible and that the deficiency is a qualitative one of the prothrombin Bendien and van Creveld (1937) of Amsterdam have isolated from fresh normal serum a substance which has a coagulating influence on haemophilic blood They have shown that this substance is almost absent from the serum of haemophiliacs This coagulation promoting substance appears to be carried by one of the protein fractions of the serum—coagulation globulin—a fraction which can be precipitated and after suitable preparation used for administration to haemophilics It can also be extracted from human placentae The clinical results so far obtained by the intravenous injection of a solution of coagulation globulin have been very encouraging

If in haemophilia one were only dealing with abnormal structure of the blood platelets haemophilic serum would not differ in any point from normal serum

Childhood is the most dangerous period for haemophiliacs for 60 per cent die before the age of 8 years and only 11 per cent reach the age of 22 (Whitby and Britten) Thereafter the severity decreases The earliest manifestation of the disease is bleeding from the stump of the umbilical cord or in some cases circumcision

Indications for blood transfusion in haemophilia

The possible uses of blood transfusion are

(a) Immediate transfusion as an active measure to arrest haemorrhage and to combat anaemia

(b) Interval transfusion as a prophylactic measure to diminish the frequency of recurrent attacks of haemorrhage

Immediate.

General Blood transfusion is the most reliable of all methods for arresting haemorrhage of an actively bleeding haemophiliac It should not be delayed too long if the more conservative methods fail If the transfusion is simply being used for its haemostatic effect, 200 c c of *citrated blood slowly introduced* will usually be as effective as larger amounts, but this is not always so It is a wise practice to obtain enough blood from the donor for two transfusions The blood should be collected into separate containers and one of these labelled and put aside in the ice chest, in case the first transfusion is ineffective or the haemorrhage recurs If anaemia is not marked, *human serum may be used instead of blood*

Local If the bleeding has not been going on for long it will be well worth while trying the local application of whole or citrated blood of the same or a different group In addition the intramuscular injection of 20 c c of whole blood of any group is sometimes effective, and much safer than horse serum the use of which makes repetition dangerous Another local application that is as successful as anything is the diluted *venom of the Russell viper*

Adrenaline should not be infiltrated locally as it has a deleterious effect upon the tissue viability, even though it may be temporarily haemostatic, and no sutures should be employed unless one can be certain that they will not cut or produce a haematoma (McFarlane, 1937)

Prophylactic

The pre-operative transfusion A haemophiliac may develop acute appendicitis or require a dental extraction in the same way as any normal person The most certain way of shortening the coagulation time in these circumstances is by a small blood transfusion—200 c c —given within twenty four hours of the declared time of the operation

Every haemophiliac should know his blood group

The interval transfusion. (Pemberton (1910), Bulger (1920), Minot and Lee (1916), Addis (1916)) Following blood transfusion the coagulation time of haemophilia is shortened

This shortening lasts only two to five days but haemorrhage does not necessarily recur immediately the effect has passed off. Because of the effect of blood transfusion upon the coagulation time it has been suggested that during childhood—the most dangerous period for these patients—blood transfusions should be given at regular intervals say every three months. Unfortunately the effect upon the coagulation time is too short to afford efficient or lasting protection so that quite apart from the tedium of repeated transfusions the method is too uncertain to be of any practical use.

If the deficiency is a quantitative one as the work of Bendien and van Creveld (1937) suggests repeated injections of human serum as they are simpler to carry out than blood transfusion may come to have a place in the prophylactic treatment of this disease.

JAUNDICE

Hepatic damage

In jaundice the coagulation time is only increased in the obstructive type and in types associated with liver damage. It is not prolonged in acholuric familial jaundice the haemolytic anaemias or in catarrhal jaundice in which the liver damage is only very slight. There is also a tendency to haemorrhage in hepatic damage unassociated with jaundice (Walters 1921) but it is naturally more often noticed in obstructive jaundice as these cases are likely to come to operation. When obstruction is due to a malignant process—with possible secondaries in the liver—the hepatic damage is greater and so is the haemorrhagic diathesis.

The importance of liver damage in the aetiology of the haemorrhagic diathesis has been confirmed experimentally by producing liver damage in animals either by ligating the coeliac artery or by chloroform or phosphorus poisoning. By these means the coagulation time of the blood can be greatly prolonged or coagulation may be prevented.

There are however other factors concerned in the production of the haemorrhage in jaundiced patients—namely, a deficiency of prothrombin and an antihaemorrhagic factor

Prothrombin deficiency.

An important contribution to the subject of the haemorrhagic diathesis of jaundice comes from the Mayo Clinic (Snell, Margath, Boland, Osterberg, Butt (1938))

Briefly their observations were as follows

i In normal blood there is a large excess of prothrombin—about 200 times the amount necessary to produce sufficient thrombin to clot fibrinogen within a few seconds

ii On the other hand, in (*a*) Obstructive jaundice, (*b*) external biliary fistula, and (*c*) conditions associated with marked hepatic damage, such as arsenic chloroform, or phosphorus poisoning, there is a deficiency of prothrombin in the plasma, and the coagulation time of the blood is prolonged

These data suggest that the presence of bile in the small intestine is in some way necessary for the formation of prothrombin, and that the liver is in some way connected with the production of prothrombin

The antihaemorrhagic factor.

The question arises as to how the bile is concerned in the formation of prothrombin This aspect of the problem has been advanced by the observations of Dam of Copenhagen (1935) He noticed that chicks deprived of certain fat soluble compounds normally contained in the diet developed subcutaneous haemorrhages This bleeding was associated with a fall in the prothrombin of the blood and was cured by the administration of the suitable diet The antihaemorrhagic substance present in the diet has been named vitamin K We have, then, two possible factors—the presence of bile in the bowel and a fat soluble vitamin—which are of importance in the maintenance of the normal level of prothrombin

Applying these observations to clinical practice, it was found that by feeding vitamin K to patients in whom bile was excluded from the small intestine, no alteration in the haemorrhagic tendency occurred But if bile or bile salts were fed with the vitamin, the coagulation time was reduced to normal even in the most deeply jaundiced patients The inference is strong, for bile acids are required for the normal absorption of fats and

sterols from the small intestine It would appear then, to be a reasonable hypothesis that the haemorrhagic tendency in cases of obstructive jaundice is due in part to the exclusion of bile from the small intestine with which the so called antihaemorrhagic vitamin K is normally reabsorbed and in part the haemorrhagic tendency would appear to be due to damage to the hepatic parenchyma as a result of which there is diminished production of the bile acids necessary for the absorption of the fat soluble vitamin

Results In 50 cases of fatal haemorrhage amongst jaundiced patients occurring in a 10 year period at the Mayo Clinic and reviewed by Boland (1938) in all but three the jaundice was produced by an obstructive lesion—most commonly neoplastic (31 out of 47) The high incidence of neoplastic obstruction as a cause of fatal haemorrhage is interesting Clinically these observations have been supported by the results of the administration of bile and vitamin K to a small series of 18 cases of obstructive jaundice at the Mayo Clinic In none of these cases did haemorrhage supervene In some within a normal prothrombin time the bile salts and vitamin K were given as a prophylactic measure but in several cases in which the prothrombin time was elevated the coagulation of the blood was reduced to within normal limits following their administration

Dosage The dosage of bile employed at the time of these investigations was 75–150 c c of human bile mixed with pine apple juice and administered by mouth before each meal Fortunately this dietary factor appears to be fairly widely distributed in nature so that the feeding of bile or bile salts alone to the type of jaundiced case referred to will usually reduce the coagulation time of the blood to within normal limits without the special addition of the vitamin The supply of the vitamin was more difficult to obtain though it can be extracted from fish meal Readers will probably be well advised to refer to the current medical literature for further information on the present methods of preparation of the antihaemorrhagic factor

Blood transfusion

From these observations it is probable that the beneficial effects of blood transfusions to cases of obstructive jaundice

is due to the introduction of prothrombin It must be remembered that although there is every hope that bile salts and vitamin K may be successful in preventing or arresting haemorrhage they cannot be expected to replace blood already lost Blood transfusion then still has an important place in the treatment of this haemorrhagic diathesis

To supply Serum Proteins

The introduction of serum proteins may be of value in

(a) Malnutrition

(b) Shock (p 170)

The treatment of shock is discussed on pp 170–3

MALNUTRITION

In *malnutrition* there is a lowered serum protein content either as a result of starvation that is to say insufficient intake or from deficient absorption as may be the case in obstructive lesions affecting the pylorus or oesophagus or destructive lesions affecting the absorption mechanism in other parts of the intestinal tract

The subject of malnutrition is mentioned as it seems that the benefit obtained in these cases from blood transfusion is by virtue of the serum protein content of the transfused blood rather than the corpuscular elements although in infants there is frequently an associated anaemia as there may also be with carcinoma of the stomach in adults The treatment of malnutrition in infants is fully discussed on p 282

The transfer of normal serum to cases of persistent vomiting such as occurs in general peritonitis has been suggested but it is questionable whether dextrose solutions are not all that is required as it appears that the tissue proteins are not utilized until starvation has been continuing for several weeks (Whipple 1933)

In *lipoid nephrosis* there is a marked lowering of the serum proteins due to an excessive loss of protein in the urine Blood transfusion has been used in an attempt to relieve the oedema associated with the condition but the effect is only transitory as the serum proteins produced are so rapidly excreted Much better results are to be obtained by means of a high protein diet

To Supply the Formed Elements and Plasma in Conditions Associated with Lowering of the Blood Volume

SHOCK

Although the physiology of shock is not yet clearly understood it is generally agreed whether it be cause or effect that the volume of circulating blood is diminished so that the problem of treating shock is inseparably connected with the maintenance of blood volume Up to the present time the only effective means of restoring the blood volume to normal is by the intravenous injection of fluid having a colloid content, and therefore osmotic tension as nearly as possible the same as normal serum If isotonic solutions are used the fluid introduced rapidly passes into the tissue spaces so that the restorative effect on the blood volume is only of a temporary nature The fluid most accurately fulfilling the necessary criteria is human blood and it should be used in preference to all other intravenous fluids if it is available

Treatment with different transfusion fluids

Blood — Serum — Gums — Sugars

Blood The time to begin the treatment of shock is before its onset This is not always possible as, for instance in accident cases where the trauma is sudden and unexpected and shock is likely to have developed before adequate treatment can be applied But when the trauma is premeditated as in set surgical operations shock can and must be anticipated and suitable measures taken to avoid it To day *no extensive operation should be contemplated* without an accompanying drip transfusion or infusion, which should be started at the beginning of the operation *and maintained until it is over or longer*

Difficulties The veins of the shocked patient are usually collapsed Valuable time can be lost in attempting to introduce a needle without cutting down in these circumstances but this is the only occasion on which dissection of the recipient s vein has preference over entry by venepuncture (except in the rare cases where no veins are visible or palpable)

Serum *Normal human serum* The use of normal serum for

restoring the blood volume in shock has the same advantages as whole blood in so far as it has the same serum protein content But in addition, owing to its diminished bulk it can be given in greater quantity In other words the osmotic and therefore the blood volume restoring properties of a pint of serum can only be obtained by twice that volume of unseparated blood, a quantity which in all probability it would be unsafe to introduce

It has been suggested that another advantage of normal serum over blood is that it can be collected and given regardless of group In practice this might lead to serious trouble if by chance the serum introduced were of high titre for example, a high titre group O serum ($\alpha+\beta$ agglutinins) given to a group AB recipient (A+B agglutinogens)

The main advantage of serum would rather appear to be that it can be stored very much longer than blood Ideally group AB serum should be stored as this could be used for all patients

The method of separating the serum (citrated plasma) Citrated blood which is allowed to stand will separate into its component layers in about three hours The clear supernatant fluid can then be poured off or drawn off with a pipette by water suction and put in separate sterile containers It must be remembered that the opportunities for contamination of the serum during the process are considerable unless a very strict technique is developed More exact methods of separating the serum are described by Thalhimer (1937) McCartney (1933) and Flosdorf and Mudd (1935)

If there is no time to allow the blood to stand and separate slowly, the preparation of serum is not a practical proposition Rapid separation of as much as 500 c c of blood requires specially large centrifuge tubes which are not available in the ordinary laboratory The serum may be stored in the ice chest at 4°–6° C

Normal serum in physiological solutions In cases of shock, instead of using gum acacia, Gottdenker in Vienna has been adding human serum to a physiological saline solution for injection The serum supplies the colloid factor in its natural form and has none of the disadvantages associated with gum

acacia which is retained more or less indefinitely in the vessels and is resistant to the ordinary processes of metabolism It was used in the proportion of 5 c c of serum to 500 c c of an isotonic physiological salt solution the exact composition of which is not disclosed The serum was not mixed with the rest of the fluid until the injection was about to begin

Gums *Gum acacia* Although gum acacia has been considerably criticized as a substitute for blood in the treatment of shock it cannot be denied that it has saved a very great number of lives Gum acacia is attacked on the grounds that it remains in the blood vessels after injection and is not excreted or broken down in the same way as other hypertonic solutions Furthermore the acacia appears in some cases to be stored in the liver where it may cause extensive damage Studdeford (1937) reports the development of a large tender liver and ultimately death in one patient following the intravenous injection of gum acacia *At necropsy there was extensive destruction of the liver resembling acute yellow atrophy* Andersch and Gibson (1933) have confirmed these observations in experiments on animals and fatal reactions have also been reported by Olivecrona (1921) and Lee (1932) and severe reactions by Diel (1935) and Studdiford (1937)

It appears also that gum acacia affects the red corpuscles It is said to interfere with their gaseous interchange and it increases the sedimentation rate It is not uncommon to find that *serum drawn from a patient who has recently had gum acacia* shows a marked tendency to pseudo agglutination

Gum acacia solutions should receive very careful preparation by an experienced pharmaceutical chemist in order to avoid contamination and to exclude impurities which have been the cause of most of the recorded reactions There is now a very good clear solution on the market All ampoules should be examined before use as after a few weeks there is a tendency for mould to grow

It is interesting to notice that Dodds and Haines (1934) have shown that the osmotic pressure of a 6 per cent solution of gum acacia in normal saline is approximately only one third of that of the plasma colloids The salt is responsible for reducing the osmotic pressure of the acacia

Contra-indications to the use of gum acacia

i In the toxaemias of pregnancy in which liver damage may already be present

ii If the infusion has to be repeated In these circumstances a cumulative effect is produced if gum arabic is used again for the second injection Extensive infiltration of the liver and cerebral embolism have been recorded after reinfusion with gum arabic

iii The upper limit of dosage is 1,000 c c

In the treatment of shock, gum arabic at present remains the best substitute for blood It seems likely however, that a serum saline solution may before long take its place

Sugars. *Hypertonic sugar and salt solutions* Ten per cent dextrose in water or hypertonic saline may be used instead of gum acacia The action of these preparations is generally not so prolonged, but if blood is not available and large doses are necessary, or if the treatment is to be repeated, they will be safer than the gum solutions

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CHAPTER XII

THE RELATIVE THERAPEUTIC VALUES OF WHOLE BLOOD AND CITRATED BLOOD

There is no reasonable or convincing evidence that therapeutic priority can be awarded to or claimed by either whole or citrated blood and it is the clinical experience of those who have used and studied both varieties that no difference exists in the results obtained

Whole blood was preferred by certain clinicians because it was thought to be

A The cause of fewer reactions of all types

B Better for the patient since no chemical had been added

C Safer in special cases for instance in the blood dyscrasias and in people who were actively bleeding at the time or had done so recently and on whom it was thought that the anticoagulant effect of the citrate might be continued

With regard to (A) there is no doubt that there was a time not very far distant when reactions in the form of chills and rigors were more frequent after transfusions with citrated blood than with whole blood and there is abundant proof in the literature that the injection of unmixed blood is rarely followed by chills This fact gave whole blood transfusion the initial advantage and consequently a long start in the competition with citrate It was felt with good reason that the extra hazard involved when a rigor followed a transfusion did not justify the greater simplicity of the technique It was necessary therefore in order to establish the citrate method as equally safe to reduce the number of reactions to a figure exactly comparable with those known to occur after whole blood transfusions

This state of affairs has now been reached and reactions following the use of citrated blood are as infrequent as those following any other method This improvement has been brought about in three ways

Firstly by the preparation of solutions—saline and citrate—with doubly distilled water

Double distillation

The use of intravenous medication in the form of dextrose or saline infusions has increased considerably during the last ten years It was everywhere noted that with the popularization of these procedures the percentage of chills increased With the use of triply distilled water a reduction in the number of chills following intravenous therapy was noticed by Rosenthal at the Mount Sinai Hospital New York and has recently been confirmed by workers at the Blood Transfusion Institution in Leningrad My own experience is that triple distillation is time consuming and unnecessary provided that careful redistillation has been carried out using in the case of a Liebig s condenser a suitable splash trap to prevent droplets of water passing over in the steam

If redistillation has been faulty there is no reason to suppose that triple distillation will improve the quality of the water distilled It is of particular importance that the water used in the preparation of intravenous solutions should have been *recently* distilled Old distilled water—however many times it may have been distilled—will cause reactions

Secondly by special cleansing of the apparatus—glassware tubing, cannulas and needles

Cleaning of apparatus

It was felt that the reaction following the use of intravenous solutions such as glucose and saline was due to the presence of some foreign protein in the water used for their preparation In spite of the careful preparation of solutions however reactions did not entirely disappear It was thought by Rosenthal that further traces of foreign protein might be present in the tubing or apparatus used and be responsible for the reactions following blood transfusion which still persisted To test this out a special department was formed at his hospital, which was made responsible for the preparation of solutions for use in blood transfusions and for the proper cleansing of the apparatus A careful technique for the latter was evolved and as a result the number of reactions which before the formation of this department had been 12 per cent, was reduced in the course

of one year (1931–2) to 1 2 per cent (331 citrate transfusions with 4 chills) It is easy to get good results immediately after a new technique has been introduced, and every member of the organization tries hard to establish a record However, a certain laxity may creep in later and spoil the results To find out whether the chills had been kept at the low level reported above further investigation was carried out in 1937, in which it was found that the same low level of reactions had been kept up, namely 1 2 per cent (653 transfusions with 8 chills) A similar but even more marked reduction in the number of chills following the introduction of this simple technique was observed by Satunof at Novgarod, who reported a drop from 53 to 2 7 per cent

Thirdly, by organizing the hospital transfusion services and concentrating the performance of transfusion in the hands of the senior members of the resident staff

Transfusion team

The extreme simplicity of the citrate method has one inherent danger It is often thought that anybody who has ever performed a phlebotomy or given an intravenous saline can successfully transfuse citrated blood In many hospitals it happens that the citrate transfusions are turned over to very inexperienced men—often the youngest member of the House Staff—whereas the other considerably more complicated whole blood methods are performed by experts The result is that in a number of clinics more chills follow the citrate method Instead of blaming the faulty technique of a poorly trained operator for these chills, the method as such has been blamed A strong opposition was thus created to the use of citrate

B With regard to the claim that unaltered blood is better for the patient Unger (1917) has published results of experiments and asserts that sodium citrate has a deleterious effect on the blood He states that sodium citrate has anticomplementary power increases the fragility of the transfused red cells and so shortens their life and decreases the phagocytic power of the leucocytes If these observations were correct the uses of the citrate method would be extremely limited, whereas in actual

fact the method has been used with excellent clinical results in the treatment of a wide assortment of diseases in which, according to this observer, bad or indifferent results would have been expected. It is enough to say that the work has not been confirmed by any other observer, and has been disproved by Ashby (1919), Mellon, Hastings, and Casey (1922).

C. In connexion with the claim that unaltered blood is better in special cases, e.g. in the blood dyscrasias, every clinician of experience has seen good results obtained with the use of citrated blood in various haemorrhagic diseases, and its beneficial use in melaena neonatorum is well known.

Paradoxical as it may seem, *sodium citrate in the doses used for transfusion work actually shortens the coagulation time of the recipient. This shortening is transitory, but definite, and the coagulation time returns to normal in a few hours.* Rosenthal and Baehr (1934) found that *the shortening of the coagulation time is due to the action of sodium citrate on the blood platelets.* These show an immediate diminution, but their number quickly returns to normal within half to one hour. Blood counts show that over 85 per cent. of the platelets have been suddenly removed from the systemic circulation. They state that there is no interaction between the platelets and the sodium citrate, but that after contact with the citrate the platelets are rapidly removed from circulation, probably by the spleen, and then destroyed; that the destruction of the blood platelets is followed by a discharge into the blood of their contents, with a resultant shortening of the coagulation time. Actual attempts to make practical use of the anticoagulant action of citrate by its intravenous injection into bleeding cases has not met with any success so far.

The fact that at Mount Sinai Hospital in New York both uncitrated and citrated blood have been used side by side for over twenty years (since 1915) afforded a rare opportunity to compare the effects in many individual cases. In a large number of patients the whole blood method was used after the citrate method had failed to effect a cure. In none of these was the clinical result superior to that following the citrate transfusion. The absence of a good clinical effect had to be attributed to the

underlying disease not to the transfusion method It is also significant that with the removal of the bogy of 'citrate reactions' the proportion between citrate and whole blood transfusion rose from being almost equally employed to about 80 to 1 in favour of citrate

In 1923 out of 143 transfusions 60 were performed by the whole blood method that is to say very nearly half Ten years later following the formation of a special department out of 477 146 were by the whole blood method and in 1935, out of 794 only 10 were performed with whole blood

Since only hypothetical advantages have so far been made for the exclusive use of whole blood a preference which cannot be regarded as being based on proven scientific or clinical data the use of citrated blood should be practised as the method of choice It is however essential in order to achieve consistently satisfactory results to follow the instructions described in detail elsewhere for the preparation of solutions apparatus and tubing (Rosenthal and Lewisohn 1933) See also further discussion in Chapter XIII Anticoagulants

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CHAPTER XIII

THE ANTICOAGULANTS

The hope of finding an anticoagulant which would simplify blood transfusion had been in the minds of research workers for many years but the substances tried out in the early days though effective in preventing the clotting of blood produced such toxic symptoms that they came gradually to be abandoned Amongst the different substances used by the earlier workers such as Braxton Hicks (1869) Wright (1891) Lespinasse (1908) were ammonia sodium phosphate oxalates hirudin and peptone

On 14 November 1914 three months after the beginning of the Great War Professor Agote of Buenos Aires performed the first blood transfusion with sodium citrate as the anticoagulant At exactly the same time Hustin of Brussels and Richard Lewisohn of New York were working experimentally with sodium citrate but it is to the latter that we are indebted for the careful work which laid down for the first time on a sound scientific basis the limitations of effective and safe dosage On 7 January 1914 Lewisohn gave his first transfusion of 500 c c of citrated blood using 2 per cent citrate to a case of inoperable carcinoma of the stomach without any technical difficulties or untoward result From this time on the method grew in popularity and with the introduction of citrate by Robertson of Toronto to the British Army in France during 1917 much valuable experience was gained and the method had become firmly established To day only a little more than twenty years later it may be regarded as the most commonly practised method In 1937 citrated blood was used almost to the exclusion of whole blood in Great Britain Denmark Holland and the U S S R In the United States in the same year out of 350 hospitals circularized by Levine and Katzin (1937) 306 were using the citrate method alone or in combination with other methods

The coagulation of the blood

There are three reasons mentioned by Sinibaldus (1642) why blood congeals on being let out of the body He quotes Hippo

crates and Aristotle "Firstly because it loses its natural heat, secondly because it contains certain 'fibrae" whose nature is cold and glutinous, and which thicken the blood, and thirdly because it is away from its natural abode and habitation, the blood as it were grieving and fearing and so thickening and congealing"

The formation of a clot is due to the action of an enzyme-like substance—thrombin, upon the fibrinogen of the plasma Thrombin is not found in the circulating blood, but is present as a precursor prothrombin Prothrombin is activated in the presence of calcium ions by thrombokinase (cephaline), a substance liberated when blood platelets disintegrate, thus prothrombin + calcium + thrombokinase = thrombin Thrombin + fibrinogen = fibrin

An alternative theory (Howell) suggests that heparin is present in the circulating blood as an antiprothrombin and that before clotting occurs, is neutralized by cephaline (thrombokinase) derived from the damaged platelets, or tissues

The Action of Sodium Citrate

Sodium citrate fixes the calcium ion—without precipitation—and thus prevents the change of prothrombin into thrombin

DOSAGE

Lewisohn (1915) found that the minimal amount of sodium citrate which could safely be relied upon to prevent the clotting of 100 c c of blood was 0 2 of a gramme of this salt To be on the safe side he used a slightly larger dose

The *dose advised* is 0 3 of a gramme of crystals of sodium citrate to every 100 c c of blood That is equivalent to saying 10 c c of a 3 per cent solution (or 1 c c of a 30 per cent solution) to be added to every 100 c c of blood

In other words if 500 c c of blood are being drawn, 1 5 grammes of solid sodium citrate will be required dissolved in a small quantity of distilled water, or 50 c c of a 3 per cent solution

Some confusion has been caused by the distribution of 3 85 per cent sodium citrate, usually in 50 c c ampoules This apparently rather strange figure was arrived at in an attempt

to produce a volume of citrate solution which would be isotonic when mixed with 500 c c of blood It was thought that weaker solutions such as 2 per cent or stronger solutions such as 30 per cent would produce hypotonic or hypertonic effects respectively upon the red cells This objection appears to be purely theoretical and has not been confirmed Hirschlaff (1936) did not find a 3 8 per cent solution to be isotonic with blood he recommends the use of 2 95–3 05 per cent sodium citrate It may be stated definitely that in the small quantities in which sodium citrate is used for immediate blood transfusion the strength of the citrate is immaterial so far as damage to vital elements of the blood is concerned

In Leningrad (1937) 30 per cent citrate was being used in amounts of 1 c c to each 100 c c and in Stockholm (1937) 10 per cent citrate in proportionate amounts of blood The advantage of the stronger solution is that the volume of fluid introduced is smaller but personally I prefer to have enough citrate to be able to wash through the donor tubing and needle before starting to introduce the blood and there is hardly enough to do this with the concentrated solutions

Toxicity

In the dosage used for ordinary transfusion work sodium citrate is non toxic Lewisohn (1915) puts the maximal safe single intravenous dose for an adult at 5 grammes Neuhof and Hirshfeld (1921) have given 6–8 grammes intravenously in a large series of cases and seen no toxic effects that is to say more than twice the amount introduced in a 1 000 c c blood transfusion No doubt this figure could be considerably exceeded if the transfusion were given slowly since sodium citrate is rapidly eliminated and this statement has been borne out by the absence of ill effects in massive citrated drip transfusions

Elimination

Sodium citrate is rapidly oxidized in the body, being excreted partly by the lungs as CO_2 and partly by the kidneys as sodium bicarbonate which renders the urine alkaline

Stability

Sodium citrate in ampoule form can be used with absolute safety up to three months after its manufacture

Sodium citrate being faintly alkaline in reaction may after a lapse of time slightly attack the glass of the ampoule This may give rise to a whitish flaky deposit settling to the bottom of the ampoule

Being a salt of an organic acid, it is liable to undergo decomposition due to bacteria or mould, so that care must be taken that complete sterilization is effected

Decomposition of sodium citrate also takes place in the presence of light if traces of iron are present

For these reasons, if the solution of citrate is not likely to be used except at some distant date it is probably safer that it should be purchased in the solid form sterile distilled water is added when it is required for use Commercially it is obtainable in either form

CITRATE AND REACTIONS

For a long time sodium citrate was blamed for the high proportion of reactions in the form of chills and rigors following the transfusion of citrated blood Some improvement followed the preparation of the citrate with doubly distilled water and the recommendation that it should be freshly prepared It was not however, until Rosenthal (1933) introduced a careful method of cleaning tubing and apparatus (p 242) that it was realized that the majority of so called citrate reactions were due to the injection of foreign protein in the form of old blood clot and debris Sodium citrate has for long enough acted as the red herring to explain post transfusional reactions and it is time that it was realized that provided the solution has been carefully prepared the cause of any reaction which may follow the transfusion should be sought elsewhere

These somewhat dogmatic statements are supported by the following observations (1) Injection of a simple sodium citrate solution intravenously is not associated with any form of reaction (2) Reactions also follow injections of other solutions if not properly prepared for example dextrose and gum saline but with the use of doubly distilled water and the careful cleansing of apparatus reactions following these also disappear (3) In a man receiving a number of citrate transfusions, reactions

are not constant, and in another series may be entirely absent. (4) As stated elsewhere the proportions of reactions following citrated and whole blood transfusions are now at the same low level—1·2 per cent (5) The percentage of reactions in citrate transfusions at the Mount Sinai Hospital, New York, fell when the organization was confined to a few operators and a special department was established for the better cleansing of apparatus, although during this time the citrate was prepared in the same way (p. 177).

(6) In large volume transfusions, relatively large amounts of sodium citrate are introduced, but no ill effects attributable to this anticoagulant have been observed by Marriott and Kekwick in over 300 large volume transfusions (1938, Personal communication).

The Practical Advantages of Using Citrated Blood

For the operator.

1. The risk of clotting is reduced to a minimum, so that the transfusion is not likely to be held up or abandoned while in progress. With whole blood it is not unusual for the transfusion to be foreshortened because of early coagulation and a smaller amount of blood given than was intended

2. The technique is simpler to acquire since speed in execution is not a factor. The method thus becomes available to a large number of operators whose practical experience of blood transfusion may be limited Popularization of transfusion in the hands of an enthusiast is thus made possible and may have its dangers, but these are certainly outweighed by other considerations.

3. No expert assistance is required. The operation can be completed single-handed if necessary This is of the greatest practical importance, and it is the most important single factor making for the success of a blood transfusion.

4. It is a cleaner surgical operation. It is unnecessary for a single drop of blood to be spilt. Probably the loss of a few c.c. of blood is of no consequence to the patient, but on occasions it considerably disturbs the operator and may influence his efficiency. In point of fact it is unnecessary and so may be taken as evidence of bad technique if it occurs

5 Most citrate transfusions once they have been started may be said to give themselves either by gravity or by syphonage

6 Transport is possible This for instance enables blood to be taken distances which will be particularly valuable if there is no donor available at the other end

7 Citrated blood can be stored

For the patient

1 Rate of introduction This can be accurately controlled and made as slow as may be desirable in the patient s interests

2 Amount introduced There is no limit to the amount which can be introduced which is dependent only upon the available supply of donors and the requirements of the patient

3 Optimum moment for transfusion If a donor has been ordered to report at a certain time—the tendency is to keep to the arrangement and to draw the blood there and then In the case of whole blood it is necessary to inject it forthwith but this may not be in the best interests of the patient If the blood is drawn into citrate it can be temporarily stored and injected when most required

4 Children Generally speaking in children under the age of one year and in infants owing to the small size of needle or cannula which has to be used citrated blood is very much easier to handle and less likely to give trouble during the transfusion

5 Drip transfusions These are not possible by whole blood methods

6 The use of citrated blood allows one to change from one solution (blood) to another (glucose or saline) as the case demands without any disconnexion of apparatus This may be of the greatest use if for instance the donor is late and it is necessary to transfuse fluid immediately Alternatively if all the available blood has been used it is possible to continue the intravenous injection with saline until another donor arrives

For the donor

1 The donor is not brought into any kind of contact with the patient If a voluntary donor this avoids what may be a

considerable trial to him If a professional donor, it prevents him from being able to recognize the patient should they subsequently meet and his intentions be undesirable or dishonest

2 If the optimum moment for injection of blood has not arrived, the donor need not be kept waiting about but the blood can be withdrawn and temporarily stored In a voluntary service it is important that the donor should not be kept away from his work for longer than is necessary or employers will begin to object

TRANSFUSOL AND SULPHARSPHENAMINE

Transfusol.

In Italy a polysulphonate of sodium, commercially known as Transfusol, is being widely used in place of citrate It is claimed for transfusol that it is less toxic than other anticoagulants and is of a particular value if the blood is to be stored Thrower in this country has tested out samples of transfusol and so far has been unable to show that it possessed any advantage over sodium citrate either in fresh or stored blood It is more expensive

Sulpharsphenamine.

In Detroit U S A , sulpharsphenamine has been used as the anticoagulant in over 1,000 transfusions The claims made for it are the usual ones—that it is less toxic than sodium citrate and that it is followed by fewer reactions (Lane 1936)

Two cases are mentioned of donors with positive Kahn tests whose blood was stabilized with sulpharsphenamine but did not apparently transmit the disease to the recipient This is put forward as a minor advantage of this anticoagulant

It has the disadvantage that it only prevents clotting for 35 minutes

HEPARIN

Heparin, 'the body's own anticoagulant', when injected intravenously into man, prolongs the coagulation of the blood for a time which varies according to the amount given It was discovered by Howell at Johns Hopkins Hospital, Baltimore, in 1928, but it was not until five years later that Charles and Scott

at the Connaught Laboratories Toronto obtained heparin in the pure state In 1936 Erik Jorpes at the Karolinska Institutet Stockholm also prepared pure heparin Chemically it is a carbohydrate, being a polysulphuric ester of mucoitin and is found in the Ehrlich cells of liver lungs and blood vessels (especially the inferior vena cava) It is particularly stable physically and chemically being obtainable at present as the calcium or sodium salt either in solution or as a dry powder The permanent place of heparin in the field of blood transfusion is problematical but it seems probable that *in vitro* at any rate it will not displace sodium citrate because it would appear to have no particular advantage over the simpler and cheaper substance

Heparin may be used as an anticoagulant either upon the donor himself or as in the case of sodium citrate by mixing with the blood *in vitro*

Heparin and the donor

In the case of a donor the injection of heparin is made into a vein of the donor who is said to be heparinized and whose blood is rendered for the time being incoagulable This would appear to be a considerable advantage and to simplify the technique especially for those operators who prefer whole blood methods In practice heparinization of the donor has been found to be without danger in 200 consecutive cases carried out at the Sabbatsberg Hospital in Stockholm In a few instances immediately following the injection the donor has had unpleasant sensations in the form of perspiration flushing and palpitation of the heart but these are transitory and infrequent It has been suggested that the donor might become sensitive to the heparin and that should he be used for a subsequent transfusion at a later date might develop anaphylactic symptoms upon receiving the second injection So far no such case has occurred and since heparin is protein free there is no real reason why sensitization should take place The sharpest criticism of the method would seem to be the risk of inducing haemorrhage in a latent bleeder or what is more likely the possibility of haemorrhage following a street accident on the way home This no doubt is a highly improbable eventuality

nevertheless, with a voluntary donor such as we are used to in this country, it is a risk that should not be taken The only way to overcome this would be to keep the donor at the hospital for approximately two hours, in other words until his coagulation time had returned to normal, before allowing him to leave—an interval of time which would not be appreciated by his employer In countries where professional services and whole blood methods are practised it may be that heparin will come to be used much more At the same time the extent to which the blood, after being treated with heparin, may still be regarded as whole blood has yet to be established

Heparin and the patient.

There is a theoretical danger in giving heparinized blood to a bleeding patient, or to any one with a haemorrhagic tendency, but the same objection has been raised against sodium citrate and has been shown to be incorrect In point of fact when given in these small amounts heparin has been shown to shorten the coagulation time of the recipient This is a constant finding (Hedenius 1937) It is to be remembered that only one tenth approximately of the heparin injected into the donor will pass over with the transfused blood into the recipient in an average volume transfusion When using heparin in place of citrate there is a quantitatively greater amount used, so that care must be taken not to exceed the dosage indicated below To be on the safe side, the coagulation time of prospective patients and possibly donors should be estimated before receiving heparin It is claimed that heparin transfusions by either method are associated with a lower percentage of reactions than when any other anticoagulant is used So far this statement has not been substantiated

Dosage

The dosage should be an amount which will allow the transfusion to be carried out without hurry yet not enough to prolong the coagulation time unnecessarily In practice, convenient and safe doses of the Stockholm preparation have been found to be

1 *To heparinize the donor*, 1 mg of heparin per kilo of body weight if injected intravenously, renders the blood taken 10 minutes after

injection incoagulable for approximately 40 minutes Direct or indirect transfusion may now be carried out by any technique

2 If heparin is used *instead of citrate* 20 mg of pure heparin (0 4 c c of a 5 per cent solution) is diluted with some sterile saline in which the blood is allowed to flow upon venepuncture Thereafter the transfusion proceeds as with citrated blood except that there is a time limit within which it must be used, or coagulation will take place

In conclusion, one might possibly forecast that heparin is more likely to find its metier in the field of vascular surgery, in connexion with embolectomy and venous grafting, in the prevention of post operative thrombosis and pulmonary embolism and possibly in the prevention of coronary thrombosis and Buerger's disease Since its presence does not interfere with ordinary blood analysis it may possibly replace the oxalates in the collection of blood samples except for the Wassermann reaction for which it is unsuited, as heparin reacts with the complement

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CHAPTER XIV

THE TRANSFUSION OF WHOLE BLOOD

THERE are two methods of transfusing whole blood—direct and indirect

The term 'direct' transfusion, accurately speaking, should be confined to transfusions by actual anastomosis between vessel and vessel This difficult surgical operation is now obsolete and recently the term direct has been applied instead to the type of transfusion in which donor and recipient, lying side by side, are in an unbroken circuit, being connected by a system of tubing with an intervening propelling agent in the form of a syringe or pump

The term 'indirect' should be reserved for those transfusions in which the operation is performed in two halves, the withdrawal of blood from the donor, and its injection into the recipient afterwards, which may be a matter of minutes or days later

DIRECT BLOOD TRANSFUSION

In the early days of blood transfusion, owing to the absence of anticoagulants, the blood could not be withdrawn outside the body The only method then available was some form of vascular anastomosis between donor and recipient, usually the radial artery of the former and the median basilic vein of the latter This method, although brought to a high level of technical efficiency by individual expert operators—notably by Crile (1907) in America—has two many disadvantages and has now been abandoned The reasons for this may be briefly stated the operation required a very considerable degree of technical ability and even then was difficult because of the small calibre of the radial artery and the risk of movement severing the anastomosis it was impossible to measure accurately the amount of blood introduced, for this quantity can only be guessed by the fainting of the donor, an improvement in the patient or an increase in his weight Clotting sometimes occurred unnoticed before the transfusion was stopped or the patient had received enough blood, or the blood might be introduced too rapidly or in too great amount On the other hand,

the injury to the donor, involving ligature of his radial artery, made it possible for him to serve only once again Apart from these difficulties, transfusion by anastomosis has been rendered unnecessary by the discovery of anticoagulants and the improvement in design of various forms of apparatus

Direct transfusion and the donor.

(i) There is a limit—about 300 c c —to the blood that can be rapidly withdrawn (especially if the donor is in a sitting position) without the possibility of the donor beginning to feel faint, an eventuality which may suddenly and inconveniently bring the transfusion to an end

(ii) In the case of a contagious disease there is the possibility that the donor may become infected by proximity to the patient

(iii) There is a risk of infecting the donor in septicaemic cases if by chance blood from the patient flows back into the syringe from which it may then be injected into the donor

In this country, where the number of voluntary blood donors' associations exceed the professional services, there has always been a disinclination to encourage whole blood transfusion by direct methods the reason for this attitude must be considered Firstly, it is argued that it is imposing too great an emotional strain upon a voluntary donor to put him side by side with a patient who may be delirious, or unconscious or may even die during the transfusion Even under better conditions than these, the heat and unaccustomed atmosphere of the sick room are more than the donor can reasonably be expected to withstand unaffected, at a time when he may already be nervous in anticipation of his own part in the proceedings For these reasons, before undertaking a direct transfusion, the condition of the patient and the temperament of the donor should be reviewed, and the latter s permission should be obtained before he is asked to serve under such conditions Various technical objections must also be raised against direct methods of transfusion They may be considered as they apply to the donor, the recipient, and the operator

Direct transfusion and the patient.

(i) With the fear of clotting always present, there is a tendency to inject the blood too rapidly this will be particu-

larly dangerous in advanced secondary anaemic cases and in babies

(ii) Slow drip transfusion is impossible

(iii) Large volume transfusion is impossible

Direct transfusion and the operator

(i) Technically the operation requires a higher degree of skill than when anticoagulants are used

(ii) The operator's attention is divided between donor and recipient either of whom may move and displace the needle A certain amount of blood is spilt which makes the operation unsightly

(iii) At least one assistant is necessary and at least two in certain methods

However as the direct arm to arm type of transfusion is almost exclusively used in France and Central Europe the advantages claimed for the method (not those claimed for the use of whole blood) will be considered

Since the transfusion is a continuous operation and not performed in two halves less preparation is necessary and there is a saving of time The blood is confined to a closed circuit and is not at any time exposed to the air and there is therefore less risk of contamination Again the blood is not allowed to cool nor is it agitated in its passage from donor to recipient Lastly this method is probably more economical since no citrate and less tubing are required

In countries where direct blood transfusions are popular the transfusion is usually obtained by some form of syringe This means of transfusing has all the disadvantages elsewhere attributed to the use of the syringe for citrated blood transfusions but in the case of whole blood these are accentuated owing to its greater viscosity The numbers and modifications of syringes are evidence of the difficulty of this method

For the expert at intravenous injection the direct method is probably the easiest and quickest way of performing a blood transfusion but it cannot be agreed that it is the safest The risk of overloading the circulation by rapid injection is too real to be overlooked nor is there sufficient latitude in the dosage the limits of which are strictly confined It is certainly better

avoided by those who are not constantly making intravenous injections It is only fair to say that from an operative point of view, the transfusions I saw in France and elsewhere impressed me by their simplicity of apparatus, the rapidity without bustle with which they were carried out, and the nonchalance of the operators

Since the principal advantage of direct transfusion, namely, the introduction of whole blood, can be equally well obtained by an indirect method, the discontinuance of its practice would appear to be justified

INDIRECT TRANSFUSION OF WHOLE BLOOD

Indirect transfusion of whole or citrated blood has been defined as one in which donor and recipient are not in physical contact or connected in any way This is the principal advantage of all indirect methods and the reason for their preference in this country However that may be, the transfusion of whole blood by any method, even by the indirect is always a technically difficult proceeding and may give trouble in the most experienced hands For this reason, owing to the readiness with which whole blood clots, speed, as when multiple syringes are used, or collection of the blood into a vessel lined or made of some anti coagulant material, is essential In addition, the blood cannot be injected really slowly, and in this limitation lies danger

Since, however, a certain number of transfusions of whole blood by an indirect method are performed each year in this country, two methods which have been found satisfactory in my experience will be described

The multiple syringe method (Lindeman)

In this method as soon as the syringe, for example a 30 c c record, is filled from the donor, it is handed to an assistant to inject into the patient, and this in turn is handed by him to a second assistant who washes the syringe in saline and returns it to the operator At first sight this chain system appears a very simple method, and as carried out at, for example, the Toronto Children's Hospital, it certainly works very smoothly. However, it is not always possible, in a hurry, to get together a team of at least three, or to have a set of syringes available and in working order

One cannot help feeling that it would be safer to transfuse by some method less dependent on speed for its success particularly in the case of babies The method is mentioned, however since it may be the only one possible in certain circumstances as for example, in the case of outlying districts where, in an emergency, no anticoagulant solution or material may be available

The athrombit apparatus.

Blood in contact with synthetic amber does not clot for a short time

The athrombit apparatus consists of a cylinder made of synthetic amber incorporating the mechanical principle of a Kimpton Brown tube The synthetic material has been named athrombit is amber coloured transparent boilable and only breakable under extreme provocation

At the present time this apparatus is the best available for the transfusion of whole blood by indirect means It works well at times but like all the methods of whole blood transfusion a straightforward operation can never be absolutely guaranteed In a reasonably extended trial I have found that the slightest technical hitch will induce clotting and that contrary to the claims of the manufacturers no time must be lost in transfusing the blood once it has been collected In my experience the claim made that clotting in the flask does not occur for 45 minutes is a misleading exaggeration In addition the container is somewhat clumsy to handle and the apparatus is expensive It is of German make, and when travelling there I had the impression that it was not widely used in that country

Paraffin wax methods [1]

The use of paraffin wax first became widely known through its application as a lining by Kimpton and Brown (1915) of Boston to their transfusion tube Slight modifications of this apparatus the chief of which have been the addition of a suction tip to aid collection and of a needle to the lower cannula like extremity of the tube to avoid cutting down on the vein have been introduced by Percy (1915) of Chicago Jeanbrau (1923) of France and Bogliotti (1932) of Turin

The Percy tube has been and still is used extensively on the Continent but is no longer the most popular method of transfusion

[1] A glass vessel thinly coated with *rubber*—the Kreiner tube—was being used in place of the Percy tube in Vienna (1937)

in the country of its invention The method has *the usual technical and clinical disadvantages* associated with the transfusion of whole blood transfusions, namely, the uncertainty of success, limited dosage, and rapid injection, and in addition certain special criticisms may be made, which have been responsible for its almost complete abandonment in this country

1 The preparation of the apparatus requires considerable time and technical skill

2 The paraffin wax is difficult to apply evenly throughout all the crevices of the apparatus, so that clotting not infrequently occurs in spite of careful attention to detail

3 The container is not rapidly sterilizable, so that it is not well suited to emergency cases

4 It is not ideal for transport as the paraffin lining is easily cracked

5 There is apt to be considerable escape of blood in its use

In addition it may be pointed out that in the pattern used most commonly on the Continent—the Percy tube—no needle fixation is possible As a result both the recipient's and the donor's veins have to be exposed by incision—a double operation requiring an extra assistant

Furthermore, if the patient is very ill and multiple transfusions are being given there comes a time when no more superficial veins are available

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CHAPTER XV

THE TRANSFUSION OF CITRATED BLOOD

INNUMERABLE patterns of apparatus and modifications of technique have been devised for the transfusion of citrated blood It is important that one particular method should be chosen from this company and developed until it is reliable in the individual operator's hands

In considering the different forms of apparatus for introducing citrated blood one can perhaps divide them according to the mechanical principle involved

The methods well established in Great Britain are

Simple	1	The *gravity* method by tube and funnel
Special	2	The injection of blood by *air pressure* using a flask and bellows
	3	The *syringe* method
	4	Transfusion with the *rotary pump*—a combination of gravity and pressure

Methods 2 3 and 4 may be regarded as special methods—as opposed to the simple gravity method—in that they consist of an apparatus specially designed for transfusion purposes only The circumstances of the case should determine which of these methods to adopt

In hospital a means of transfusion must be taught which can be widely applied and which does not involve buying expensive or elaborate apparatus For this reason the simple gravity method must hold pride of place particularly in teaching institutions

Outside hospital, when for instance a transfusion has to be carried out in a patient's home difficulties of transport and assistance will make it advisable to use one of the more easily operated special forms of transfusion apparatus The best of these is the rotary pump

Transfusion by the funnel gravitation method and by the rotary pump will now be described in detail Transfusion by the other methods is not advised for the reasons given on pp 228–31

THE GRAVITY METHOD OF TRANSFUSION (TUBE AND FUNNEL)

The name of this method is so firmly rooted in the past that any attempt to change it would be unavailing In principle the method still remains the same though the conical funnel is no longer used, but has been replaced by a graduated glass cylinder

The Advantages

Although new methods and modifications are constantly displacing one another, the tube and funnel so far has outlasted them all It is in use in most of the teaching hospitals in London and I found it to be the most widely practised method wherever citrated blood was used in Europe and North America The reason is that it is simple—simple to prepare and simple to use The component parts of the apparatus are in the possession of every doctor, so that there is nothing to buy and nothing to lose that cannot be easily replaced A continuous even flow is obtained which can be regulated with a fine degree of accuracy Once the needle has been introduced the transfusion may be said to give itself

However, the method is not popular on all sides and it has recently been described in a leading medical periodical in the following terms I venture to suggest that the gravity method of blood transfusion is obsolete and when used is sheer cruelty to the nurse who stands with arms aloft ' As will be pointed out later some method of suspending the container so that it need not be held is the most important preliminary to this method of transfusion

The Criticisms

The criticisms that are made from time to time are that

An open method is undesirable Certainly an open method of introduction may be violating a surgical principle but the fact remains that blood is actually bactericidal to the ordinary organisms in the air So far as it has been possible to ascertain no cases of infection resulting from the exposure entailed by pouring the blood into a container have been described in the literature

The blood is not introduced at body temperature If the blood is given at a fast drip or as a continuous stream and is warmed to 104° Fahrenheit before being poured into the funnel it will be introduced approximately at body temperature since it will not have had time to cool more than a few degrees on its way down the tubing If on the other hand the blood is introduced slowly drop by drop there is no need to warm it (p 249)

Air locks increase the technical difficulties Troublesome air locks do occur even in practised hands but with a little care and patience these can nearly always be overcome particularly if the syringe method of entering the vein is used (p 204) and if an air lock in the form of a glass dropper is included in the length of tubing

The glass container for the blood has constantly to be refilled This can readily be avoided by using a container large enough to hold all the blood to be injected

One or more assistants are required By using a stand to hold the container an assistant becomes unnecessary

For one reason or another it is indeed unusual to see a transfusion with tube and funnel go without a hitch but this is the fault of the transfuser rather than the method Lack of knowledge in regard to points of technical detail and the association of too many assistants are the common causes of difficulties in the execution of this method which will now be described

The Transfusion

Apparatus required (Fig 24)

The apparatus required is seen in the accompanying diagram

The container At this point it will be as well to draw attention to the tendency to use a container with a relatively small capacity—about 200 c c—for the tube and funnel type of transfusion This has the disadvantage that it requires constantly refilling during the transfusion Furthermore it cannot be adapted for large volume transfusions To avoid reduplication of apparatus for two methods which are in principle the same (small and large volume transfusions) it will be simpler to standardize a container for all intravenous work A graduated

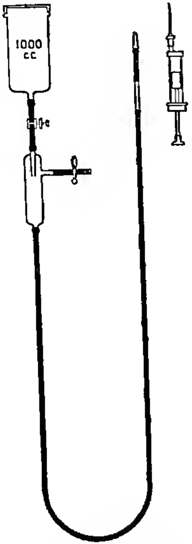


Fig 24 Apparatus for simple gravity transfusion

container of capacity 1 000 c c will hold enough for a small transfusion without being unnecessarily bulky, and can easily be adapted for a larger volume transfusion for which it will be capacious enough as it is undesirable in the latter to have more than one donor s blood in the container at a time (p 250) Most doctors possess some form of douche can which is readily adapted to a gravity transfusion In addition by using almost the same apparatus for all types of intravenous infusion an opportunity is afforded to those interested to become familiar with a very adaptable technique

The glass dropper (visible feed) If available a glass dropper should be included as this supplies visible evidence of the rate and progress of the transfusion The bulb also makes a very convenient air trap

The syringe Whatever pattern of syringe is used it is important that it should be fitted with an *eccentric* nozzle This fitting enables the needle to be introduced with the syringe parallel to the skin instead of at an angle

The stand A suitable stand for holding the container is described on p 239

Technical success in transfusion largely depends upon

The development of a *single handed* technique

The *stabilization* of the two extremities of the transfusion tubing that is to say the needle in the vein and the container holding the blood

Having assembled the apparatus according to Fig 24, the operation is started by securing the container

THE TECHNIQUE

First stage—Stabilization of apparatus

(i) It is important in the gravity method that the *glass container should be suspended* and not held Every ward has an adjustable stand designed for holding containers for intravenous and rectal drip saline If there is no such stand available the container can very easily be strapped to a screen or to the wall at a higher level than the arm

(ii) The next step is to pour warm normal saline into the reservoir until it comes out bubble free at the distal end The

tubing should be held up so that it forms a U bend In this way all air will be displaced and air locks will be prevented When no more air bubbles pass the glass window the controlling clip is screwed up tight The tubing is now laid aside and a suitable vein selected

(iii) The selection of a vein In this type of transfusion as opposed to a large volume transfusion it should be possible in the great majority of cases to introduce the blood without cutting down upon a vein Venesection should be necessary only in cases of collapse with veno spasm and in fat subjects The antecubital fossa will usually be found to provide the most suitable vein For a more detailed discussion of this matter see p 261

(iv) The *skin* is prepared with spirit in the usual way and some form of *compression* is applied to the arm proximal to the vein selected (see p 248) A small wheal is then raised with *novocain* and massaged away

Second stage—Intravenous puncture

There are three practical methods of venipuncture

1 RECORD SYRINGE AND TUBING ADAPTOR

Any record *syringe* that the operator is accustomed to handling may be used It should be one with an eccentric nozzle and with a capacity not greater than 10 c c or it becomes too bulky to manipulate with accuracy

The *adaptor* should be of the male variety and attached to the end of the transfusion tubing

The *needle* selected may be an ordinary serum needle or one fitted with a Strauss shield (p 4) It is introduced attached to the nozzle of the syringe

Comment This is not an entirely satisfactory method as some blood is necessarily lost during the change over, but it has the advantage that no special apparatus is required Unless special care is taken the needle will be displaced during the manipulations It is for this reason that control of the needle should be maintained throughout with artery forceps rather than with the fingers My attention was drawn to this important practical point by a Canadian colleague, Dr J Turner of Toronto

Procedure

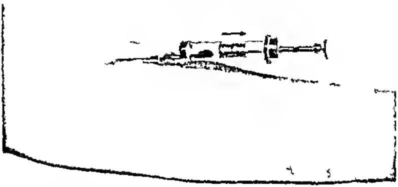


Fig 25

1 The needle is introduced into the vein Accurate intravenous puncture is confirmed by withdrawing blood into the syringe The syringe may be used empty but personally I prefer it to be half filled with saline as this makes it easier to decide when the vein has been entered

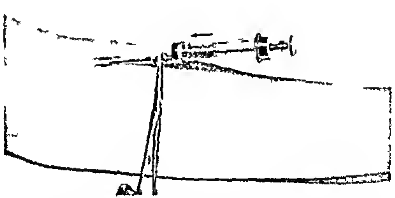


Fig 26

2 The arm band is loosened and the contents of the syringe re-injected to confirm that the vein has been cleanly entered

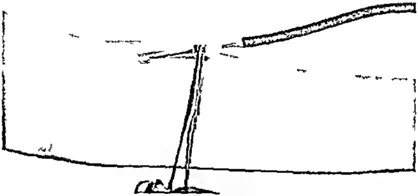


Fig 2

3 The change over is now made The needle in the vein is held firmly and accurately in position with a pair of *artery* forceps until after the change has been effected The syringe is detached The tubing is picked up with the free hand and the male adaptor at its extremity is fitted into the butt end of the needle

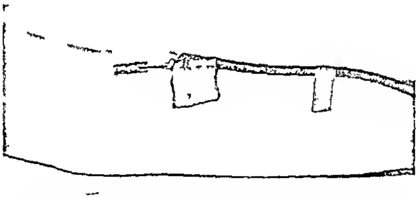


Fig 2

4 The joint between needle and adaptor is secured to the arm with adhesive strapping
5 The controlling clip below the container is unscrewed
6 Only when the operator is satisfied that the saline is running without obstruction as shown by a steady drip in the glass dropper and by a fall in the level of the saline in the reservoir should the blood be added to the container and the drip rate readjusted by means of the screw clip

II SYRINGE AND TWO WAY TAP

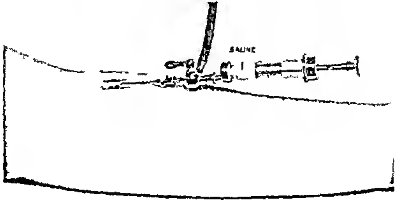


Fig 19

Procedure

(i) The two way tap is attached to the extremity of the transfusion tubing The standard pattern of tap is adapted for record fittings

(ii) The selected needle and syringe (5 c c with eccentric nozzle) are fitted to the two way tap (Fig 20)

(iii) The needle is introduced into the vein Intravenous puncture is confirmed by withdrawing blood into the syringe

(iv) The arm bandage is loosened and the contents of the syringe re injected to confirm that the vein has been cleanly entered

(v) The two way tap is turned so as to put saline needle and vein into continuity

(vi) The controlling clip below the container is unscrewed

(vii) As soon as the saline is running satisfactorily the needle and tap are secured to the arm by a transverse piece of strapping and the syringe is carefully detached

Comment No blood need be lost by this method It has the disadvantage that a small piece of special apparatus is necessary and that this must be strapped to the arm with the needle It is a little clumsy

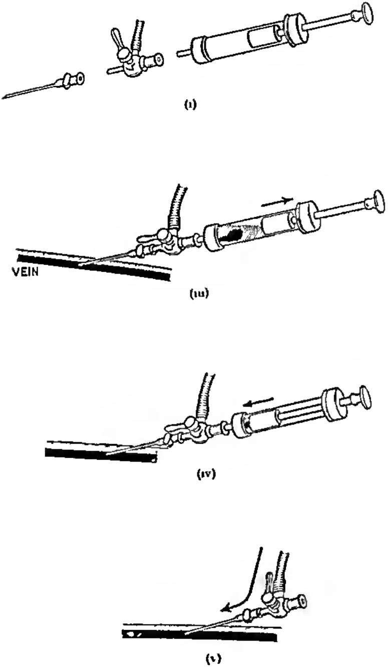


Fig. 30

III SYRINGE WITH A SIDE ARM

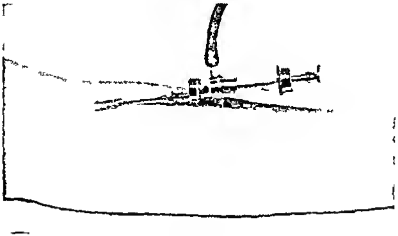


FIG 11

Procedure

When a syringe with a side arm is used the transfusion tubing is filled with saline as before The side arm of the syringe is then attached to the end of this tubing with the plunger pushed home The venepuncture is made and confirmed by withdrawing blood into the syringe The plunger is withdrawn up to the level of the side arm On passing this level the saline is put in connexion with the syringe and on the release of the controlling clip will flow through the syringe into the vein The syringe with plunger *in situ* should be strapped to the arm The speed is regulated by the screw clip

Comments There are several minor disadvantages of this particular method

(i) The weight of the tubing attached to one side of the syringe gives an unfamiliar balance to the intravenous manipulation

(ii) A special syringe is required

(iii) The syringe cannot be removed after the intravenous puncture but must be strapped to the limb

A method to avoid. It occasionally happens that a nurse is asked to hold the funnel and compress the tubing, while the needle—attached to the distal end of the tubing—is thrust into the vein When the needle has been inserted the nurse lowers the funnel below the level of the selected vein and releases the tube Blood will then flow back if the vein has been successfully entered if not, it is compressed and raised again Raising and lowering of the funnel is continued until the vein has been entered Owing to the alternate compression and relaxation of the tubing there is a chance that an *air lock* will hold up the flow or that some *saline will escape* into the tissues round the vein and obscure it If the container is stabilized and the vein entered by one of the methods already described these mechanical interruptions can be avoided The need for the additional assistant is avoided by stabilizing the funnel and by doing the operation in two stages, the needle being inserted first and then connected up to the rest of the apparatus

TRANSFUSION WITH THE ROTARY PUMP

TRANSFUSION with the rotary pump combines the advantages of an apparatus capable of exerting a positive pressure with those of the simple gravitation method

Excellent as the simple gravity method is for most purposes there are occasions when it is essential to be able to exert a controlled positive pressure This is particularly necessary in cases of collapse—when the vein may be in spasm and offer resistance to the inflow of fluid—and in transfusing infants

Quite apart however from these absolute indications for the exertion of a positive pressure during injection the general conduct of any transfusion is greatly simplified by means of a rotary pump if there is one available

The pump fulfils the following criteria which may nowadays be demanded of a special transfusion apparatus

The propelling agent

(i) The propelling agent should be ready for use at all times and should not require *sterilising* or *assembling*

(ii) It should be so constructed that there are no *detachable parts* which might get lost or interchanged

(iii) As far as possible it should be *indestructible* and not subject to mechanical failure

A special transfusion apparatus should also fulfil the following general principles

(*a*) It should be possible to operate the method *single handed*
to introduce the blood at a *drip rate*
to exert a definite *positive or negative* pressure whenever desired
to *change* over at any time to the injection of another fluid such as glucose saline solution

(*b*) It should enable a clean surgical operation to be performed

(*c*) Once started the transfusion should continue *automatically* if desired that is to say by gravity or syphonage

Apart from fulfilling these conditions an important feature of the pump is that it allows a *constant negative pressure* to be

maintained while the attempt at venipuncture is being made This point is explained later (p 222)

DESCRIPTION OF THE PUMP

The description.

The pump consists of an aluminium casting the centre of which is bored out so as to form a well with straight sides, 2 inches in diameter and 1 inch deep

In the centre of the base of the well is the rotor The lower end of the rotor is in the shape of a circular disc which can be rotated by means of a crank handle at the upper end Between the crank handle and the disk revolves the roller which compresses the rubber tube against the wall of the well The spindle on which this roller revolves is provided with eccentric end bearings for the purpose of varying the pressure on the rubber tube

The principle

The principle of the pump is merely the action of a cylindrical roller massaging a rubber tube backed by a solid, smooth sur

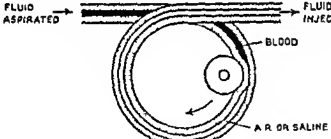
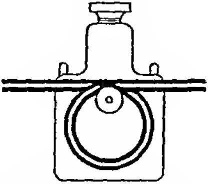


Fig 32 The principle of the pump

face As a result two chambers are formed in the tube, one on each side of the point of contact of the roller It will be readily understood that as the roller moves along the length of the tube, the chambers will vary proportionately in volume The chamber behind the roller will increase in volume and suction will be produced The chamber in front of the roller will be reduced in volume and compression will be obtained By looping the tube in a cylindrical cup in which a roller revolves from a central axle, the same effect is produced in a more limited space

The drip adjustment

A rotary pump was described by Noel in 1876 and a more recent model has been elaborated by the French engineer Henry



The drip adjustment

VICE CLOSED. Tubing is compressed between the roller and the wall of the well. Flow of blood stopped.

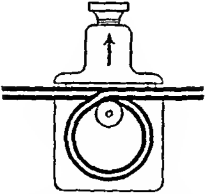


FIG. 33. VICE OPENED: Pressure on the tubing is released as the adjustable segment of the wall of the well moves away. Blood will now flow by gravity.

(1936). The latter's hand pump, known as the Henry Jouvelet apparatus, was intended for direct arm to arm transfusions; it was not designed for transfusions at a drip rate for which it is unsuitable. It is also necessary to work this machine by hand

continuously throughout the transfusion These and other disadvantages made this particular apparatus unsuitable for the transfusion of citrated blood

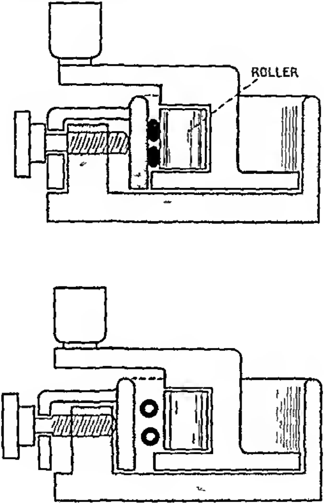


Fig 33A

The new pattern of rotary pump seen in Fig 33 has been devised so as to allow of *automatic* transfusion at *any* rate of flow This has been achieved by making a section of the wall of the well movable

A segment of the wall forming the well is adjustably mounted

on a projection of the base and the radial movement of this segment is controlled by a screw. The reason for this adjustment is twofold. firstly it serves the purpose of introducing the rubber tube into the well and clamping it in position in the two lateral channels which enter the well at a tangent. Secondly the screw adjustment acts as a drip regulator when the roller remains stationary opposite the movable segment.

In use the pump may be steadied by screwing it to the operating table or a side table such as the patient's locker. A more practical arrangement than this is to combine pump and bottles in such a way as to form a transfusion unit.

THE TRANSFUSION UNIT

In spite of centralizing the equipment considerable delay can still take place before a transfusion is under way. This is due to the disjointed nature of the usual transfusion apparatus—the propelling agent, the bottles, the tubing, the thermometer—each forming a separate item.

This disadvantage can be overcome *by combining the various components into a single unit*. In this way the efficiency of the method is appreciably improved, the technique is simplified and the apparatus stabilized.

Such a unit is readily arranged when the pump is used as this does not require sterilizing. By fixing the containers at one end of a small board and the pump at the other, the transfusion unit seen in Fig. 28 is produced. In this manner is formed a strong, stable platform from which the transfusion can be directed without interruption.

The bottles are secured by means of spring clips which project from either side of a central strip of metal carrying a scale graduated in cubic centimetres. By having a scale in this position, the expense of graduation is avoided when using the standard capacity 20 ounce screw capped Winchester bottles for both saline and blood. The spring clips are so placed in regard to height that they grip the bottle neck immediately above the shoulder. In this way the bottles are held down as

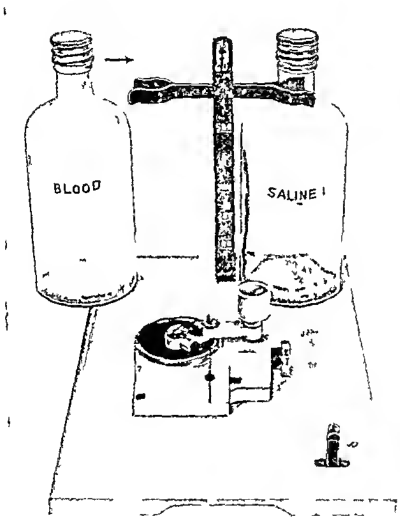


Fig 34 The transfusion unit

well as in so that there is no rattling in transport The unit is covered by a lid which has a removable box occupying the space over the pump in which extra apparatus such as tubing and instruments can be carried In this way all dead space is obliterated

TECHNIQUE OF TRANSFUSION WITH THE ROTARY PUMP

The Apparatus

Sterilization The different pieces of apparatus described below should be kept assembled as a unit and sterilized. They readily make up into a small compact parcel.

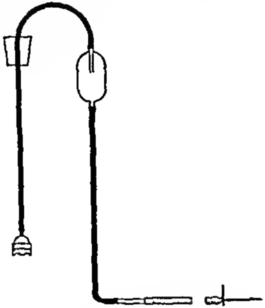


FIG. 3. The recep[illegible] the various components seen in the diagram—with the exception of the needle—are fitted together [illegible]. Each set is then [illegible] into a sterile packet and stored. The needle is sterilized separately [illegible] boiling.

Components The apparatus required for a transfusion in the order in which it is assembled will be:

Recep[illegible]	
Collapsible tubing 2 inches	
Glass window	Assembled and
Pressure tubing [illegible] feet	kept in a
Glass dropper	sterile packet
Rubber bung	
Filter	

In addition there will be required

> The transfusion unit with rotary pump
> Screw cap bottle—blood,
> Screw cap bottle—glucose saline

and the usual requirements for local anaesthesia and skin preparation

General considerations

The tubing should be of sufficient *length* to allow the pump to be raised well above the level of the vein selected It should be *pressure* tubing of a size which can be accommodated by the pump (see p 241) Ordinary tubing is not satisfactory in the pump The tubing should be sterilized by boiling (p 242)

The glass window should be placed *close* to the needle The union is effected by a very short piece of collapsible tubing This plays a special part during venipuncture (p 223) It sometimes happens that the observation window is separated from the needle by six inches or more of tubing In such a case, in order to confirm the point of entry of the needle into the vein, blood must be withdrawn through a greater length of tubing than is necessary, which increases the risk of clotting

The filter and dropper If necessary the transfusion can be performed without the weighted filter or the dropper but both should be included if available, particularly the visible feed

If no weight is used, the end of the tubing resting on the bottom of the bottle should be notched so that when suction is made it will not stick to the bottom of the glass

If no dropper is used the rate of flow must be determined by observing the level of fluid in the bottle The output per revolution is also constant, being approximately 1 c c , but this is an unnecessarily tedious method of calculating the volume injected

Glucose saline. Isotonic—glucose saline or simply normal saline may serve several purposes

(i) By filling the tubing with this solution rather than with blood at the outset a translucent medium is provided at the level of the observation window, so that when blood

is drawn from the vein it can be clearly seen This is a point of great practical importance in making a successful venipuncture, and it also makes the operation cleaner and avoids any possible wastage of blood

(ii) By starting the transfusion with glucose saline the optimum moment for introducing the blood can be selected

(iii) In an emergency it may be advisable and is sometimes very useful to be able to begin the transfusion with glucose saline while waiting for the donor to arrive (p 233)

THE TRANSFUSION

After the preliminaries of sterilization and assembling have been completed the procedure is as follows

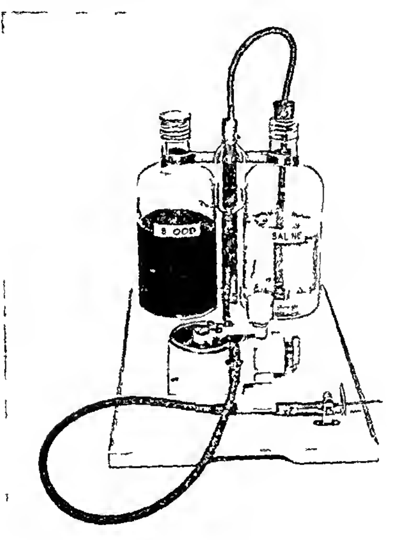


Fig 36 Loading the transfusion unit

Loading (Fig 36)

1 The weighted filter is lowered into the saline bottle
2 The needle is kept sterilized by placing it in the clip provided
3 The tubing is looped into the well of the pump and the vice closed

4 The handle of the pump is turned in a clockwise direction to displace all the air in the tubing until saline drips from the end of the needle and no more bubbles pass the window

A suitable vein is selected and some form of proximal compression applied to the limb The overlying skin is prepared and a small wheal raised with local anaesthetic

Injection (Fig 37)

The injection is now ready to begin with the tubing still in the saline

5 The needle is inserted and as soon as it is thought that the vein has been entered

6 the operator s free hand turns the handle of the pump through half a circle in an anti clockwise direction Blood will immediately flow into the window if the needle is in the vein

7 The pressure bandage is now slackened and the injection of saline begun

8 Only when the infusion is seen to be proceeding satisfactorily is the tubing transferred from the saline bottle into the blood the injection being stopped while the change over is made

If a two way tap is included in the length of the tubing there is of course no need to stop the transfusion while the tap is switched across from saline to blood

9 The needle should be secured in place with a piece of strapping

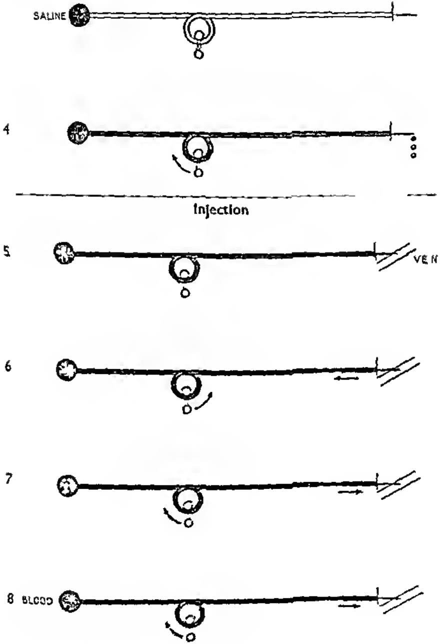


Fig. 3

Continuation of the transfusion

The transfusion may now be continued by hand or by gravity. To continue by gravity it will be necessary:

(1) To raise the blood and the pump (the unit) to a higher level than the selected vein, the height depending on the resistance to the inflow, which in turn depends chiefly on the bore of the needle employed.

(2) To turn the handle of the pump to the mid position (Figs. 36, 42), as in any other position it will obstruct the tubing.

(3) To unscrew the vice until the required rate of flow is obtained.

FAILED VENIPUNCTURE

It is always best to attempt a difficult venipuncture in three stages.

If after inserting the needle beneath the skin (Fig. 38) negative pressure is made, the tubing between the needle and the window will collapse (Fig. 39) as the result of the suction exerted when the pump handle is turned. Without removing the point of the needle from the tissues its position can be changed until the lumen is successfully negotiated. With the entrance of the needle into the vein the walls of the collapsed tubing suddenly distend and blood is seen in the window (Fig. 40). This deliberate collapsing of the tubing is a most helpful manœuvre.

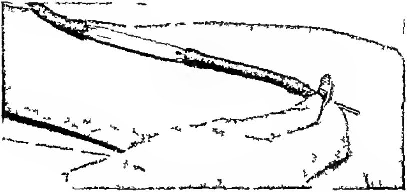


Fig 38 (i) Insertion of the needle beneath the skin then

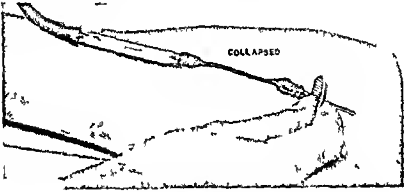


Fig 39 (ii) exertion of a negative pressure followed by

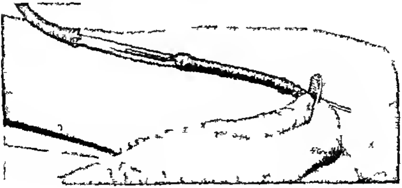


Fig 40 (iii) the actual attempt at venipuncture

MANAGEMENT OF THE TRANSFUSION WITH THE ROTARY PUMP

The handle

Short transfusions

Once the needle is in the vein the handle of the pump need not be used again except in those few cases in which it is necessary to make a positive pressure throughout the transfusion for example to overcome venospasm in a shocked patient In the majority of transfusions the handle of the pump is merely used as a convenient instrument to start the transfusion which is thereafter continued by syphonage at a drip rate

Long transfusions

In a long transfusion it is an advantage to be able to exert positive pressure from time to time during the course of the transfusion In this way the tubing can be flushed through at intervals so that any tendency to clot formation or obstruction is diminished Once every hour after first closing the vice the handle should be turned three times in a clockwise direction once every six hours the tubing should be transferred for a short time (*15* to 30 minutes) to saline

Temperature control

For transfusions at a *drip* rate that is to say the majority of transfusions there is no need to heat the blood in the container above room temperature level It is good practice however to bandage (over cotton wool) the last six inches of tubing to the patient s arm so that all the body heat available may be transmitted through the tubing to the blood just before it enters the patient

In the few cases of *rapid* transfusions the blood bottle should be kept in a bowl of water at 104° F until the blood is required for injection—that is to say until the vein has been entered and the saline is running without obstruction

The blood bottle is then fitted to the unit and the tubing lifted over from the saline In a transfusion of 500 c c given in twenty minutes to an exsanguinated patient—the blood will probably not require heating again during the injection—if given more slowly the blood can be stood throughout in a bath of water at a temperature not exceeding 104° Fahrenheit

Rate of flow.

The flow depends upon the vertical height of the container above the vein selected and upon the resistance produced peripherally by the needle and vein

The rate of flow is regulated by the screw on the movable portion of the pump

The range is wide—from a rapid continuous stream to a few drops a minute

Sedimentation of corpuscles

On standing, the red corpuscles sediment to the bottom of their container Although this is not a matter of very great practical importance, the passage of concentrated corpuscles only is likely by increasing the viscosity of the blood to induce earlier clotting than would occur if the cells were mixed with the supernatant serum

The mixing of cells and serum may be brought about in two ways

(1) *By hand* The blood bottle in the transfusion unit is removed from its clip and gently rotated till mixing is complete This should be carried out systematically every half hour, it only takes a moment or two

(2) *By bubbling oxygen through the blood* The arrangement for this mechanical method of continuous aseptic stirring of the blood is seen in Fig 41 The cork is fitted with a small piece of glass tubing for the withdrawal of the blood, and with a standard Clover's ether dropper which provides the oxygen inlet and outlet

DIFFICULTIES

The difficulties met are all due to actual or partial obstruction Air locks do not cause trouble by this method

Slowing of the drip-rate.

If the drip rate slows or stops, there is either an insufficient head of pressure to maintain the flow, or there is an obstruction Before assuming that an obstruction is present the height of the transfusion unit should be checked

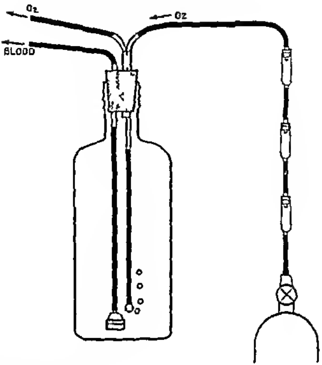


FIG 41 Method of bubbling oxygen through the blood to prevent sedimentation of corpuscles

(1) The height of the transfusion unit

To maintain a satisfactory flow the bottle of blood in the transfusion unit should be at least two feet above the level of the selected vein If raising the unit does not restart the flow there is probably an obstruction present

This may be due to

(i) a tight bandage or strapping proximal to the point of entrance of the needle which will require loosening or removing

(ii) the weight of the bed clothes pressing on the tubing or the limb This can be relieved by rearranging the bedclothes and by the use of a cradle

(iii) kinking or overlying the tubing

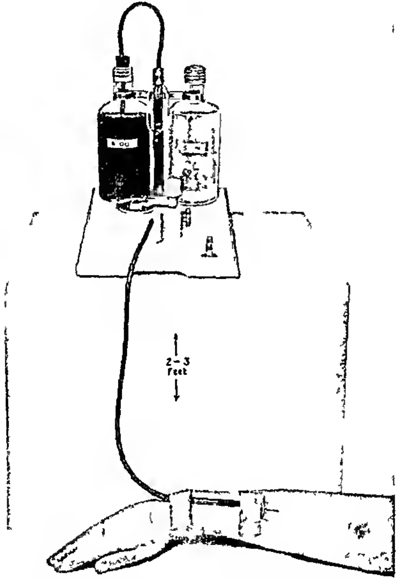


FIG. 42. *A transfusion in progress.* The tubing is now in the blood bottle. The needle is in a forearm vein. The transfusion unit is raised on a side table. It is usually more convenient to do this by means of the slotted rod fitting seen in figs. 46 and 51.

(iv) The handle of the pump being away from the mid position, in which case the tubing will be directly obstructed by the roller

(2) Obstruction in the filter.

(i) The fine mesh of the filter may be blocked by clot If this is suspected the transfusion should be temporarily stopped without withdrawing the needle, the filter is then removed While the filter is being cleaned the transfusion can be continued by transferring the tubing to the saline bottle

(ii) The filter may be resting on a portion of clot at the bottom of the bottle To test this raise the filter and if the flow restarts it will be unnecessary to do any more than suspend the filter so that it is clear of the upper surface of the clot

(3) Obstruction in the needle.

(i) *Malposition* Before assuming that the needle is blocked the position of *the limb* should be altered—for example at the elbow some degree of flexion is usually advisable If the elbow is fully extended I have noticed that there is a tendency to intermittent obstruction

If changing the position of the limb does not restart the flow the position of *the needle* should be examined The shaft of the needle may be lying obliquely to the length of the vein instead of in the same line or the point of the needle may be directed against the anterior wall when it can be felt beneath the skin This fault can be corrected by placing a small pad under the hilt of the needle, which by raising this part depresses the point

(ii) *Clot* If the flow does not restart after checking the possible causes enumerated above, the handle of the pump should be turned gently in a clockwise direction Obstruction is shown by a rise in the level of blood in the drip bulb In the case of true obstruction the needle must be removed, *the tubing washed through with saline* to clear it completely of blood and the transfusion started afresh by introducing the needle into another vein, preferably in the opposite limb

SYRINGES

With most transfusion syringes there is a two or three way tap by means of which the syringe is connected on filling with the blood, and with the patient's vein on being evacuated

The types include the three way direct flow, Rotanda Jubé—used in Great Britain—and Tzanck, Oehlecker, Unger, Soresi—patterns used elsewhere

I had an experience of over two hundred transfusions with the special blood transfusion syringes before giving up this method My reasons for abandoning the syringe method are given below

General criticisms

1 *Multiplicity of parts* A syringe manufactured in this country has eight parts five of them vital If one of these is forgotten or lost or has become interchanged with another syringe of the same pattern the transfusion cannot be given by that syringe In addition these multiple parts take time to assemble

2 Syringes have to be *sterilised*—if this is not done until immediately before the transfusion the glass barrel must be left some time before it will be cool enough to fit the plunger

3 Syringes may *break* or crack while boiling to sterilize while in use if any strain is put upon the joints while cleaning after the transfusion or in transit

4 Syringes are expensive to repair and replace Replacement of the glass barrel of one pattern of syringe costs 12s 6d

5 An *assistant* is usually required It is not easy for any one inexperienced with special blood transfusion syringes to do the transfusion without help

6 *Many syringes are of foreign make and representatives who* have undertaken to do repair work are few and far between and usually out of the spare part when it is required In many cases the syringe has to be sent abroad which involves an irritating delay

7 The *all metal* syringe is not a solution of the problem since these syringes dent which is even worse than breaking Another disadvantage of the all metal syringe is that the blood cannot be seen during injection

Disadvantages during the transfusion

(i) The blood cannot be introduced at a *drip rate*

(ii) The flow is *intermittent* not continuous and it cannot be observed

(iii) The transfusion *is not automatic* as the syringe has to be held and worked throughout The result of this is fatigue and a tendency to give the transfusion too quickly

(iv) Syringes *stick* This can be a very serious matter and may involve abandoning the transfusion Jamming may still

occur in spite of careful cleaning, the use of liquid paraffin, and assembling while cool

(v) Syringes *leak* This does not matter very much, but it is unsightly

METHODS OF INTRODUCTION USING BELLOWS (AIR-PRESSURE)

Positive air pressure as a means of introducing blood was first employed by Robertson (1918), whose 'bottle was a familiar sight in hospitals towards the end of the War It was later improved by Keynes (1920) and this apparatus has in turn been modified by McCartney (1935)

The principle of these methods is to create a positive pressure in the flask or bottle used by means of bellows attached to a side arm The pressure exerted on the surface of the blood displaces it through an outlet tube from which it passes by way of a length of tubing to the patient

The flask and bellows method was not chosen as the special method for detailed description in this book as in practice I have found it to be less reliable than the rotary pump Although the bellows method works very well in the hands of those who are used to it it is not widely used in this country to day

The difficulties that may be met with in the course of a transfusion will now be mentioned

1 The assembly of the apparatus has to be made in *relays* there are three stages (*a*) filling of the intermediate section with saline (*b*) insertion of the needle into the patient s vein (*c*) connexion of intervening segment, distally to the needle and proximally to the air lock It is not altogether easy to do this single handed and the apparatus can only be assembled immediately before use It cannot be set up before arriving at the patient s house

2 There are multiple joints each of which is a point of insecurity

3 Two accurately fitting rubber bungs are required If the apparatus is not very frequently in use the rubber stiffens and is no longer air tight either at the sides or at the central perforation On one occasion in my experience when the bung was produced after a long interval, it could not be used on

account of the stiffening McCartney (1933) has overcome this particular difficulty by substituting a metal screw cap carrying an inlet and outlet tube in the place of the rubber bung This has the advantage that it is a standard fitting, and so will last indefinitely

4 If too great a positive pressure is raised within the flask the rubber bung will blow out If at the end of the transfusion the positive pressure within the flask is not first released before withdrawing the needle from the vein a considerable escape of blood will take place If the level of the blood is not noticed towards the end of the transfusion it is possible that it may all be injected and be followed by the air in the flask, with the possibility of air embolism

SUMMARY

(i) Transfusion by a gravity method is the simplest and safest method of transfusion for general use

(ii) In special circumstances it will be quicker and more practical to use an apparatus designed solely for blood transfusion purposes

(iii) The special apparatus selected for a detailed description as being the most reliable is the rotary pump

(iv) The efficiency of the pump is increased by uniting it with the other components of the method, so as to form a co ordinated transfusion unit

(v) The disadvantages of methods depending upon air pressure and injection by syringes are outlined

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AN EMERGENCY TRANSFUSION

Blood transfusion in common with most surgical procedures, is rarely *ab initio* a matter of grave urgency It becomes an emergency, however if the occasion should find us unprepared or if we are asked to give the transfusion at the last moment Delay in decision or delay in execution may thus create an emergency state where one should not have developed By keeping the outfit ready packed for use no time is wasted in sterilization and assembly The true emergency transfusion is most often required for trauma

The exact procedure to be adopted will naturally depend upon whether or not there is available a donor of known blood group and this in turn will depend upon the existence of a transfusion service in the district

There is a transfusion service

(*a*) **The patient is in hospital** The patient should be typed and a donor of the appropriate group obtained from the transfusion service

In no circumstances should it ever be necessary for a hospital to ask for a member of the so called universal donor group because 'there was no time to group the patient' The blood group can be determined in under five minutes and the delay is not long enough to prejudice the life of a patient who is likely to respond to blood transfusion

(*b*) **The patient is not in hospital** Telephone instructions

(i) To clear the patient s room as far as possible of all unnecessary furniture

(ii) To prepare a room next door for the donor

(iii) To get in communication with relatives who may be required as donors

It is good practice to go to the patient s house as soon as possible This gives one the best opportunity of assessing the severity of the haemorrhage and the need for immediate action In the majority of cases the urgency not unnaturally, is greatly exaggerated Outside the operating theatre there are few occasions when a blood transfusion must be given within the hour When, however, in the opinion of the operator the case

appears to be one of genuine urgency and the patient is some distance away he will be well advised to arrange for a donor of the universal donor group to be sent direct to the patient's home before he himself sets out. To omit grouping in these circumstances is justifiable as, owing to the time lost in travelling, there must otherwise be considerable delay before the patient's blood group can be known and a donor obtained. If the urgency is not great, however, the recipient should be grouped and cross matched with the donor in the ordinary way.

If the donor has not come by the time I have arrived at the patient's home and there is clearly no time to be lost, it is my own practice *to begin the transfusion*—or rather infusion—*with glucose 5 per cent*, or *glucose saline*. If it is necessary to cut down, this should also be completed while one is waiting, and the cannula tied in. Then, when the blood has been collected, all that remains to be done is to add it to the saline. If the transfusion unit is being used the plunger filter is taken from the saline bottle and placed in the blood.

There is no transfusion service.

If there is no transfusion service or panel of donors, the patient's friends or relatives must be relied upon. Relatives are to be preferred to friends as they are more likely to be compatible.

In an emergency there will be no time to exclude syphilis except by questioning and by clinical examination, but together these methods are very reliable. The Kline exclusion test can be completed in two hours if there is an expert available (p. 90).

The subsequent procedure will depend upon whether typing serum is available or not.

If typing serum is available, the patient should be grouped and a donor of the same group or group O selected.

If no typing serum is available, a reasonable quantity of the recipient's serum should be collected by withdrawing blood from a small vein into an hypodermic syringe. By mixing the separated recipient's serum so obtained with a drop of whole blood from each of the prospective donors, the compatible donors can be selected and the others rejected, without knowing the blood groups of any of the individuals concerned.

Note (i) It is as well to remember that a blood transfusion can only be accelerated up to the point when the blood starts to run into the patient after that no further expediting is possible or legitimate, in view of the dangers associated with speed shock overloading, and rigors

(ii) If there is no citrate or other anticoagulant available, the blood should be defibrinated This can be achieved quite efficiently with a sterilized fork

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CHAPTER XVI

APPARATUS

THE CENTRALIZATION OF TRANSFUSION EQUIPMENT

Transfusion personnel.

ALTHOUGH blood transfusion is now a comparatively commonplace event, the preparation involves, in comparison with other operations of the same category, a disproportionately greater number of individuals and more disturbance Some dissipation of personal effort cannot always be avoided, nor is it necessarily desirable that it should be, but the more individuals involved the more opportunity there is for delay and for error It is by no means unusual for the determination of the blood group to be made by a pathologist, the collection of blood by a resident medical officer, the cross matching by a house officer, and the injection given by a surgeon This arrangement is convenient in a large hospital where transfusions are frequently performed and where supervision and help are readily obtained, but in smaller institutions and in practice away from hospital the system is as unsound as it is unsafe

Transfusion equipment.

In or out of hospital much time and energy can be saved by keeping the necessary apparatus and solutions for transfusion sterilized and ready for use, in a cupboard (Fig 43) reserved for the purpose in some accessible ward or operating theatre As far as possible the apparatus (tubing, dropper, glass connexions, &c) should be sterilized *in an assembled* form, so that when required it is not necessary to fit the different parts together

COLLECTING BOTTLE

The Advantages of Standardization

In visiting different London hospitals to see transfusion work, one of the most striking differences I noticed between each was in the type of bottle or flask used as a container for the blood There was a great variety of these, no two hospitals using the

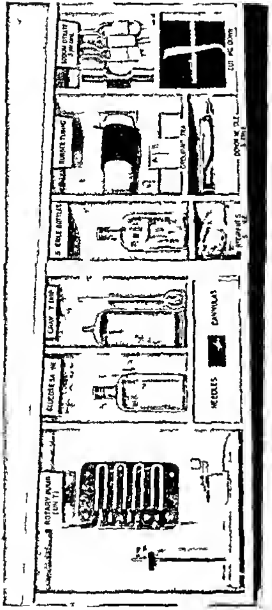


Fig. 43 Centralization of the transfusion equipment in a cupboard

same shape or size or obtaining them from the same firm The majority of containers were hand made, which from the economic point of view is unsound, because the cost of a glass vessel is much greater when hand blown than when it is cast from a mould, since in the former case production of the flask involves more labour Again, with the hand made bottle, varying quantities of glass are taken up each time so that its capacity and the inside diameter of the neck are not constant The practical outcome of this is that a rubber bung which will fit one bottle tightly will fall through the mouth of another

Fig 44 The screw capped —pint size—Winchester Bottle

It is desirable then, both from the point of view of expense and to obtain uniformity of size and capacity, that the particular transfusion bottle chosen should be of a pattern that is manufactured in large numbers

The Screw-cap Bottle

The bottle which appears to fulfil most closely the required conditions is the 20 ounce screw capped Winchester bottle (Fig 44) This pattern is already being used in many of the larger London voluntary hospitals and throughout the London County Council hospitals as a standard container for intravenous solutions (McCartney, 1933)

The committee of consultants appointed to the British Red Cross Blood Transfusion Service has also provisionally selected this bottle as the most suitable for the storage of blood in the event of the outbreak of hostilities It is mass produced in a large range of different capacities—although the pint size is the most suitable for transfusion work—and it is made in plain and amber coloured glass The bottles cost a few pence each They are manufactured by the United Glass Blowing Company Another excellent container is the well known wide mouthed dairy milk bottle

The screw cap

I think that it is particularly important that the glass rim surrounding the mouth of the bottle should be protected from dust collection This is most effectively achieved by means of a screw cap which covers the whole of the dangerous area (Fig 44) The alternative arrangement in which the mouth of the bottle is closed with a glass stopper or rubber bung allows dust to collect on the rim whence it may be displaced into the blood during the act of pouring from one vessel to another (Fig 45) The screw caps are made of aluminium are lined with cork or rubber and are very cheap

FIG 45 An illustration to show where dust may collect in relation to the rim of a stoppered vessel

Sterilization

Preliminary washing New bottles should always be washed and boiled before use This is because new glass may yield alkali On filling a new bottle with distilled water shaking and allowing to stand the pH of the contents may be just on the alkaline side but after a single boiling these bottles rarely yield more alkali

Autoclaving A pint bottle containing 70 c c of sodium citrate should be autoclaved at 5 lb pressure for 40 minutes If a higher pressure than this is used the citrate breaks down into a very fine crystalline powder The stopper should be closed when autoclaving with a solution in the bottle

INTRAVENOUS STAND

Stand for suspending a glass container (Fig 46)

The majority of intravenous stands consist of some form of tripod which stands on the floor and has a hook like upper extremity from which the container is slung by means of a metal ring and bucket handle This forms a very unstable piece of apparatus as the tripod may be knocked out of position

by any one passing the foot of the bed while the container swings precariously in the air

I have found that a stable and practical form of intravenous stand consists of

(a) A *hollow* steel rod slotted at its upper end
(b) A *universal* clamp by which the rod may be attached to a bed, side table, or dressing trolley
(c) A *frame* for holding the container The frame consists of a hollow cylinder carrying two incomplete metal rings At the upper end of the cylinder is a transverse bar which fits into the slot on the top of the steel upright

Note

(i) The height of the container is varied by adjusting the position of the rod in relation to the universal clamp
(ii) A spring clip—similar to a trouser clip—may be used instead of the upper metal ring It has the advantage that it prevents any rattling and it also allows for small variations in the size of the neck of individual containers In my experience it does not stretch or lose its spring
(iii) The platform on which the rotary pump is mounted carries a small fitting which enables the transfusion unit to be carried by the steel rod described above

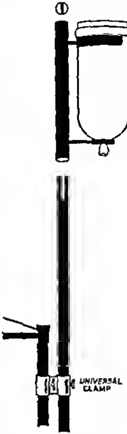


Fig 46 Intravenous stand The frame holding the container fits over the slotted metal rod (St George's Hospital pattern)

GLASS DROPPERS

For transfusion by gravity. (Fig 24)

The Laurie type of glass dropper *with side arm* is the most suitable (p 270) When this pattern of dropper is used for

blood transfusions it needs to be considerably larger than the standard size available which is suitable for saline infusions only This is because the continuous dripping of the blood produces a column of froth which may interfere with the flow if the narrow type of dropper is used

A small piece of rubber tubing carrying a clip is attached to the small glass side arm If the fluid or froth in the bulb rises and threatens to obscure the point of the dropper the procedure is as follows First the controlling clip below the container is screwed up tight and then the side arm clip is removed and sufficient air is allowed in to displace the fluid in the bulb to within half an inch of its lower extremity (p 270)

The side arm is also useful for overcoming air locks If by any chance the clip comes off accidentally in the course of the transfusion the blood will simply overflow through the side arm There is no danger of air embolism

For transfusion with the rotary pump (Fig 30)

For transfusion with the rotary pump a smaller glass dropper than the above is more convenient and there is no need for the inclusion of a side arm The point of the dropper should be made of such a length that it is at least $\frac{3}{8}$ inch away from the side of the bulb or bubbles of air may in bursting carry the blood from the dropper on to the side wall of the bulb down which it trickles so that the rate of flow cannot be determined

RUBBER TUBING

Pressure Tubing and Non-pressure Tubing

There are two main varieties of surgical rubber tubing which differ only in their consistence—(a) a comparatively thin walled type which is easily compressed between the fingers and (b) a stout thick walled tubing usually called pressure tubing which although compressible requires considerably more external pressure to do this

Pressure tubing

For transfusion purposes the thick walled tubing is the best because it is less likely to become kinked or obstructed by the

patient overlying it. The dimensions advised for use with the pump or for large volume transfusions are

Internal diameter $\frac{5}{32}$ inches
External diameter $\frac{9}{32}$ inches

Pressure tubing also has the advantage that it is much more durable and so can be used repeatedly provided Lewisohn and Rosenthal (1933) method of cleaning it is meticulously observed.

Collapsible tubing

The collapsible tubing can be of great value if it is used to join the glass window to the recipient needle (p. 223). In this position, particularly when using the rotary pump, the tubing can be made to collapse by creating a negative pressure once the needle has penetrated the skin. The tubing re-expands immediately the needle enters the vein lumen. This manœuvre greatly simplifies difficult intravenous punctures and avoids haematoma formation (p. 223).

Donor tubing

The tubing used for the withdrawal of blood from a donor should have a relatively large bore, but the tendency is to use it both too wide and too long. The tubing seen in Fig. 1 has an internal diameter of $\frac{3}{16}$ of an inch.

New or old tubing

The question arises whether fresh tubing should be used for each transfusion. This has been advised by some and blamed as a cause of transfusion reactions by others. In my own experience it makes no difference whether new or old tubing is used *provided that* it is prepared as outlined below. For some time I used new tubing as a routine, but more recently I have been doing an average of three transfusions with each length of tubing before destroying it.

Tubing which has been used for collecting or giving *whole* blood and tubing used in large volume transfusions should never be used twice.

Cleaning of tubing before use

If new tubing is blown through *a cloud of French chalk* will be produced. It is for this reason that tubing should always be

washed through and *boiled* before it is used for the first ti
Autoclaving may sterilize the powder but will not remov

Procedure—based on Rosenthal and Lewisohn s descrip (1933) New or used tubing should be treated as follows

1 After each transfusion separate all parts—tubing gl ware and filters—and *syringe through with cold tap water* remove fresh blood

2 Wash in a dilute solution of *soft soap* This removes bl stains from the outside of the tubing

3 Rinse thoroughly in *tap water* to remove soap

4 *Place all parts in a large pan containing* sodium hydrox (0 1 per cent solution) and boil for five minutes This disso old clot or debris remaining in the lumen

5 Transfer to a bowl of *distilled water* to remove the sod hydroxide

6 Wash again with doubly *distilled water*

After this the parts are ready to be assembled and sterili either by boiling or by baking in the autoclave

Sterilization

No rubber tubing autoclaves very satisfactorily It is vulc ized in the process and becomes hardened and angulated possible then it should be sterilized by boiling

Storage

Rubber tubing is perishable so that unless it is going to in almost daily demand a limited amount should be obtained a time Long lengths are very conveniently kept on a wood roller perforated at either end to secure the extremities (I 43)

Colouring agents

Surgical rubber tubing is made in different colours—r green, black, white and transparent The transparent tub has the advantage that one can see when it is clean and it d away with the need for a glass inspection window The dif ences in colour are explained by the use of different dy antimony sulphide for red carbon for black chalk and z oxide for the white chromium oxide for the green

The *red tubing* is the most pliable and therefore the best for transfusion purposes. Zinc oxide in the white tubing makes it somewhat stiff to manipulate. It is important that surgical rubber tubing should be sulphur free or it will not be resistant to boiling with alkali, such as soda.

BLOOD FILTERS

Is filtration necessary? A large number of transfusions are given without filtering, apparently without harm. When clots occur large enough to be stopped by a filter, they have formed because insufficient anti coagulant was added. In other words, clot formation can be prevented. In practice a large clot will be too big to pass into the tubing and a small clot will be held up in the narrow bore of the needle, so that embolism is very improbable.

The addition of a filter, however, is so simple that it is well worth including if only to avoid arrest of the flow during the course of a transfusion by obstructing clot.

When giving blood by the gravity method it may be strained through a square of muslin, silk or cotton or nickel gauze, when blood is being introduced by other means, the filter must be incorporated somewhere in the tubing. The most convenient type is the Luer Lok combined filter and sinker which can be attached to the extremity of the tubing to be let down into the bottle (Fig. 35). Such filters serve a double purpose, as they prevent the tubing rising above the level of the blood as the bottle empties, and so *filling with air*. *Home made filters* can be manufactured by using a bundle of capillary tubes which can be made to adhere with a Bunsen flame or simply by tying a small piece of muslin round the end of the tubing.

Filters in the course of the tubing, usually in the form of glasswool, are unsatisfactory. They introduce two further joints into the system, are readily broken, and difficult to clean satisfactorily.

NEEDLES

There is one essential about a needle and that is that it should be *sharp*. For continued success in intravenous work it is absolutely necessary that the needle should be *resharpened after each*

time it is used This can easily be done by the operator himself on a small stone the size of a microscope slide

There are two main types of needles from which to select

1 Parallel sided needles (Record)
2 Tapering needles (French)

Parallel sided Needles

The parallel sided needles of the serum type are to be preferred to tapering needles since they are the ones which are in general use and consequently easier to handle

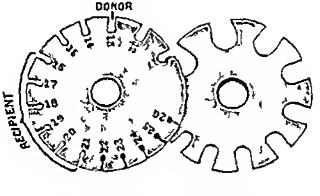


Fig 47 The standard wire gauge (S W G)

The most useful addition to such a needle is the standard *Strauss shield* This is a genuine help as it gives an excellent grip and being a standard fitting is readily obtained Any particular needle which the operator fancies can have this shield incorporated (Figs 2 and 3)

The lumen of the needle should be greater with the donor needle than with the recipient Generally speaking *both are used in sizes which are larger than is necessary* For the **donor** needle size 13 (Fig 2) and for the **recipient** needle size 16 (Fig 38) (of the standard wire gauge (Fig 47) each 28 m m in length are satisfactory) Smaller needles (sizes 17 22) should be used for patients with small veins

Some confusion exists with regard to the various numbers allotted to needles to differentiate their size There are two gauges the coarse standard Birmingham wire gauge sizes 1–26 (Fig 47) which is applied to

the larger or serum range of needles and the hypodermic needle gauge, sizes 1–20 (3–11 are missing) The scales do not overlap and are in no way connected though the largest in the hypodermic scale approaches in size the smallest in the serum scale The hypodermic scale is particularly misleading, there being no definite increase each time from size to size, *in fact two sizes may vary in length of shaft only and have the same bore* The missing numbers were manufactured at one time but dropped when it was found that there was no demand for them

The end of the needle *should not be too pointed* or it will tear or perforate the posterior wall of the vein In other words the bevel should be short though it should have well cared for cutting edges It is of no consequence whether the bevel faces upwards or downwards as long as it is sharp

Some needles are *shaped* so that the butt end is bent away from the skin when it is lying in the vein the object being to prevent pressure on the arm at this point This is more comfortable for the donor or patient, but the needle is not so easy to introduce, and is not advised

Tapering needles

Tapering needles, the best known of which is French s are for the most part of unnecessarily large bore, and in my opinion their use should be discontinued With a needle of so large a bore it is necessary to nick the skin with a scalpel a practice which is open to abuse, and the needle itself is not easy to grip or to introduce Furthermore, certain donors complain that as the needle is pushed upwards into the vein some pain is caused in spite of a local injection, due presumably to stretching of the unanaesthetized vein wall by the broader base end of the needle For these reasons this type of needle is not advised

The needle-cannula.

It has been suggested that the sharp point of a needle, if left in a vein for any length of time, may, by traumatizing the endothelium, initiate thrombosis To obviate this, certain operators (Waring, 1938) prefer to use a needle cannula, the needle portion being inside the cannula and having cutting edges which project beyond the end of the cannula The needle portion is withdrawn as soon as the vein has been entered, leaving the blunt-ended cannula in the lumen It is question

able whether this instrument really effects what it claims, and it is definitely not quite so simple to insert

Sharpening.

I am indebted to A Dickson Wright of St Mary s Hospital, London, for the following description (1935)

The needle is inserted obliquely through a cork so that the bevel appears on the rounded surface of the cork Then a special needle hone of Arkansas stone is drawn lightly across the bevel till the whole ring of the bevel glistens Then the needle is pushed farther through the cork and the edges lightly stroked with the needle stone to remove any feathering of the edges which may be present Finally, the needle is removed from the cork and drawn lightly over the finger to be sure that there is no crochet hook at the tip of the needle and if this is present it is smoothed off with the stone With such treatment a perfect point is assured and this makes injection infinitely easier

If the usual needle taken at random in the theatre or ward is inspected with a magnifying glass and compared with a sharpened needle the advantage of honing the needle is made clear

Storage

Between transfusions the needles should be kept in a 3 per cent chloroform paraffin mixture (3 grammes paraffin wax in 100 c c chloroform)

CANNULAS

Cannulas will only be required when cutting down is necessary They may be made of metal or glass Glass cannulas are to be preferred as it can be seen when they are clean If the cannula is to be left in the vein for any length of time or if the patient is restless or unconscious some form of *shaped* variety should be used Shaping of the cannula is designed to prevent the cannula slipping out of the vein and to avoid pressure on the skin A good pattern is Siggers s (1939) modification of the Kekwick (1937) cannula This has a bulbous expansion near the extremity to prevent the cannula slipping out of the vein and an angulation of the shaft to avoid pressure on the skin (Fig 48, and Fig 59, p 267)

Fig 48 *Cannulas*[1]
Upper Siggers s modification of the Kekwick cannula
Lower Kekwick cannula

[1] Obtainable from A L Hawkins 15 New Cavendish Street, W 1

The metal variety has the advantage that it is unbreakable and can be drawn out into a very fine point which makes it a convenient type for using with infants As this cannula is not transparent debris may be left in the lumen unless it is carefully cleaned For very young infants the cannula portion of the Waring or Bateman type of needle cannula or the very small cannulas used for experimental work on animals are useful—for example a cat cannula

GLASS CONNEXIONS

A glass connexion should always be included as an observation window close to the needle It serves two *purposes*

(i) In starting a transfusion blood can be drawn back as far as the window to confirm that the needle is in the vein

(ii) Any air bubbles which may enter through a leaking joint or elsewhere will be seen as they pass this observation point

Y-shaped glass connexion

If the supply of blood is not immediately available or if it should run out it will be very useful to be able to keep the injection going with saline or glucose saline until blood is available By means of a Y shaped connexion this is made possible without discontinuing the injection

A two way tap is sometimes used instead but they are more expensive and less reliable as the tap joint is not always air tight—with the result that air may be sucked in or blood leak out

TO PROCURE VENOUS OBSTRUCTION

For the *donor* the sphygmomanometer is quite the best way of obtaining venous obstruction, as it produces an even and constant distribution of pressure It should always be used

For the *recipient* a yard of wide bandage (5 in) is required It is put round the arm as seen in Fig 49 the two ends being held by the patient or an assistant and released when the vein has been entered It is more efficient than the hand alone less painful than rubber tubing and less disturbing to an ill patient to place in position than a blood pressure bag

An excellent *armlet* (Dickson Wright 1935) is obtainable which combines an air pressure bag to compress the vein anteriorly and a length of Goodge splinting in which the forearm lies By a strap over the wrist the movements of the forearm are effectually limited which is particularly helpful in a nervous or delirious patient

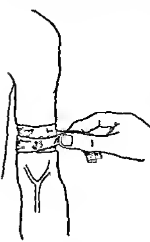


FIG 49 The band go tourniquet

TEMPERATURE CONTROL OF THE BLOOD

A When withdrawing the Blood

It is definitely unnecessary to maintain the temperature of the blood while it is being collected as is sometimes attempted by holding the receiver in a bowl of warm water or by taking the blood into a thermos flask It is now known that cooling the blood for a limited period has not a harmful effect

Blood which has been allowed to cool should be brought up to the required temperature gradually taking five minutes to raise 500 c c from room temperature to body temperature If the blood has been taken from a refrigerator a correspondingly longer time should be allowed

B When Injecting the Blood

In a continuous stream If the blood is entering the circulation rapidly that is as a continuous stream it should do so as nearly as possible at body temperature Fortunately these rapid injections are becoming less frequent since it is appreciated that they are rarely justified (p 143) and with their disappearance the need for accurate heat control diminishes

The temperature of the blood should never be raised above 104° Fahrenheit If the container is placed in a bowl of water maintained at this level the blood taken from it will under average conditions enter the patient at body temperature the exact fall in temperature as it passes down the tubing depend

ing upon the length and thickness of the tubing the rate of flow, and the external temperature

If the blood bottle is placed in a reasonably *large* bowl of tap water at 104° Fahrenheit at the beginning of the transfusion, it will be safe—from the point of view of temperature—to give 500 c c of blood in twenty five minutes without adding to the water

If a smaller bowl is used it will be necessary to add hot water to it from time to time, and to prevent overflowing some water will have to be removed For this reason it is much simpler to stand the blood in as large a bowl as is practicable

The temperature is more accurately maintained by a simple immersion heater or thermostat placed in the bowl or tank surrounding the blood but for most purposes this is unnecessary

Drop by drop

I have expressed the opinion elsewhere (p 143) that I believe that the majority of transfusions however small the volume of blood to be transfused, should be given at a drip rate Not only is this a safer method of introducing blood but it has an additional advantage, for if the blood is being introduced drop by drop, there is no need to warm it This is the clinical observation of all those who have had experience of drip transfusions whether they be of small or large volume Flowing at this slow rate the blood, by the time it reaches the end of the tubing is at room temperature whatever temperature it may have been when it left the container Methods of heating therefore such as hanging hot water bottles round the container or enclosing it in a special water bath are quite unnecessary

The temperature of the fluid as it passes through the last few inches of the tubing should, however, be raised if possible, and this is best done by bandaging the last six inches of tubing to the patient's skin (Fig 60) *By this means the body heat may be utilized to raise the fluid within to body temperature just before it enters the vein This can be aided further by placing a hot water bottle or electric pad close to the limb above the point of entry of the blood*

More important, however, than any of these attempts to raise the temperature of the transfused blood, is to make

certain that the patient is himself warm and not unnecessarily exposed during the injection' (Bailey 1934)

Overheating the blood.

A fatal result of a blood transfusion apparently due to over heating the blood is reported by Professor S L Baker (1937)

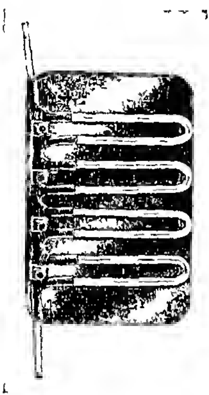


FIG 70 The drip regulator (Marriott and Kekwick)

The blood was kept standing in a receptacle surrounded by a water jacket the temperature of which was about 130° F The patient developed all the typical features associated with a severe intravascular haemolysis and died in the renal phase a fortnight after the transfusion

As emphasized above blood should never be heated to a temperature higher than 104° Fahrenheit and this will only be necessary if it is to be injected at a relatively rapid rate

THE DRIP REGULATOR

Marriott and Kekwick in a personal communication give the following description of their drip regulator ('drip clip')[1]

The drip regulator was invented because of the fluctuation in rate which is produced by the use of a screw clip on rubber This fluctuation is due to the very small size of the orifice in the rubber tubing at the site of constriction The new regulator substitutes a longer resistance of small bore The regulator consists of four glass U tubes

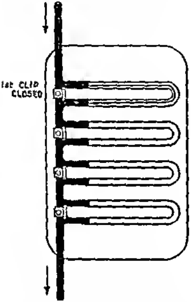
[1] The drip regulator can be obtained from John Bell and Croyden Wigmore Street London

joined together by branched rubber tubing, the whole being stabilized by fixing to a metal plate (Fig 50)

Transfusion with the drip regulator (Fig 51)

The blood reservoir is first suspended in the ordinary way at least three feet above the selected vein

The drip regulator is introduced into the length of tubing below the glass dropper



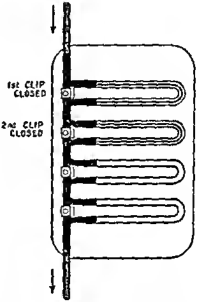


Fig 51 The drip regulator the upper clip has been closed so that the blood travels through the first U tube and then vertically downwards

The drip regulator the first and second clips have been closed so that the blood travels through the corresponding U tubes and then vertically downwards

The tubing and drip regulator are filled with saline—the saline being manœuvred through the U tubes in turn by closing the various clips

The rate of flow.

When all the screw clips are open an uninterrupted swift flow of blood passes into the vein The closure of any one clip so that it completely occludes the tubing forces the blood to go round the glass U tube This gives a rate of approximately 40 drops per minute when the container is fixed three feet above the

vein The closure of two clips puts two U tubes into the circulation and gives a drip rate of 20 The closure of all four clips gives a rate of 10 After a time this rate slows up to about 7 owing to the sedimentation of corpuscles in the rubber tubing above Even slower rates can be obtained by lowering the height of the container There is some difference between individual clips but these can be easily overcome by altering the height of the container

Should any one of the U tubes become blocked or the drip slowed, the nurse can be instructed to open all the clips so that the whole weight of the column of blood comes on to the vein and when it has started to flow easily to use another U tube

The end of the transfusion

As soon as the transfusion has finished the regulator is disconnected from the tubing A 20-c cm syringe is attached to one end after it has been filled with water All the screw clips are left open The water is forced through the by pass tubing several times until no more blood issues from the other end Now one screw clip is fastened down and more water is forced through so that the corresponding U tube is cleared of blood The by pass is then recleaned This is repeated with each U tube which has been in use until the apparatus is completely cleared of blood This latter point is important It is much easier to clean the apparatus immediately the transfusion has finished than after it has been left for an hour All the screw clips are now left open so that the apparatus is then ready to be resterilized

SUMMARY

1 Centralization of the transfusion equipment sterilized and assembled ready for use will simplify transfusion by any method
2 The pint size Winchester screw capped bottle is suggested as a container for the blood The advantages are that it is a standard product with a uniform capacity it is made of good quality resistance glass and it is cheap
3 A glass dropper is described which enables one to regulate the fluid level

4 Attention is drawn to the difference between ordinary rubber tubing and pressure tubing
5 The method of cleaning and sterilizing rubber tubing is described
6 The use of a filter is advised A combined plunger filter is described
7 The importance of resharpening needles after each transfusion is emphasized The actual type of needle is of secondary consideration
8 A shaped glass cannula designed to remain securely in the vein in cases of prolonged transfusion is described
9 The value of a glass connexion as an observation window is pointed out
10 Methods of obtaining venous obstruction are described The use of rubber tubing for the purpose is condemned
11 The temperature control of the blood is discussed The need for careful control is greater when the blood is being injected as a continuous stream, less when only at drip rate

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CHAPTER XVII

TRANSFUSIONS OF LARGE VOLUME

A TRANSFUSION of large volume may be defined as one in which the blood of more than one donor is used For practical purposes this means any continuous transfusion of more than 600 c c

INDICATIONS

It is difficult to lay down absolute indications for large volume drip transfusions, but so far as one can see at present they are clearly indicated in the following circumstances

As a pre-operative measure

I When operation is necessary in a patient whose blood must be raised to a safe operative level *rapidly* This may occur in

(a) Patients who are *actively bleeding* and require operation to arrest the haemorrhage Examples include bleeding peptic ulcer—bleeding uterine fibroids The object of the transfusion in these cases is to maintain the blood volume in the face of continuous blood loss until such time as the bleeding stops spontaneously, or can be stopped by operation

(b) Patients who are severely anaemic and in whom an emergency surgical condition arises, for example, appendicitis occurring in pernicious anaemia or any other severely anaemic state

II When operation is necessary in a patient whose blood cannot be raised to a safe operative level by means other than blood transfusion that is to say, in patients who do not respond to iron or liver therapy, for example

(a) Before splenectomy for certain conditions associated with anaemia namely, splenic anaemia, thrombocytopenic purpura Gaucher s splenomegaly

(b) In patients who are bleeding relatively slowly but too rapidly for iron therapy to keep up with the haemorrhage, for example before radical operations for malignant conditions associated with anaemia, as in carcinoma of the stomach or colon

During prolonged operations

In prolonged operations associated with continuous slight blood loss for example extensive intracranial operations

Fig 59 Transfusion during operation The rate is most conveniently regulated by the anaesthetist He is in a position to observe the blood loss and general condition of the patient and can vary the rate accordingly The arrow points to the drip adjustment

abdomino perineal resection of the rectum and certain gastrectomies The object here is to restore the blood loss and so counteract shock

To take the place of multiple transfusions

In aplasia and hypoplasia of the bone marrow treatment by multiple transfusions is very tedious for the patient A single

large volume transfusion at the outset will greatly reduce the number of attendances necessary

MANAGEMENT OF DONORS

I **The responsibility of providing donors** must be firmly placed upon the relatives and friends of the patient and it should be pointed out that the transfusion cannot be undertaken unless the donors are forthcoming from this source The repeated use of service donors for large volume transfusions would very soon disorganize a transfusion service

II **Instructions to donors** All the prospective donors should be told to come to the hospital *at the same time* and to meet in a prearranged place A whole day s work can be upset if the different volunteers arrive at odd times for examination

III **The direct compatibility test** If a number of people attend the quickest way of selecting possible donors will be by cross matching the various donors cells with the recipient s serum Those who are incompatible can be sent away The remainder may be of the same blood group as the patient or they may be members of group O

IV **Blood grouping** The compatible donors should now be grouped It is necessary that the donors finally selected should all be of the same group as one another for if they are not and their bloods are mixed in the reservoir agglutination will occur for example if the patient is group A it is not permissible to mix group A blood and group O blood in equal proportions in the reservoir although both may be compatible with the patient

V **Donors of the same blood group as the patient** are to be preferred if available In practice this will usually be possible if the patient is a member of either of the commoner groups i e A or O If the patient is a group AB or B it is likely to be difficult to find several members of the required group in which case if the patient is seriously ill it will be justifiable to transfuse with the blood of a series of donors of group O

VI ***Test for syphilis*** *Syphilis should be excluded in all* the donors unless there is some very good reason for neglecting this precaution The test used—Kline Wassermann &c — will depend upon the time available (see p 90)

It is sometimes practicable to collect the blood for transfusion and for the Wassermann reaction at the same time When this is the case it is convenient to pierce the collection tubing close to the donor with a hypodermic needle, and to withdraw the necessary amount of blood into a syringe

APPARATUS

It is important at the outset to emphasize that a large volume transfusion does not involve the use of any specialized apparatus It is convenient, but not essential to make certain small additions to stir the blood and so prevent sedimentation but they in no way alter the principle, which is that of the simple gravitation method already described Large volume transfusion involves the application of a new principle in dosage and not a new technique for administration

Apparatus required (Fig 53) (based on Marriott and Kekwick's original description)

1 An oxygen cylinder fitted with a pressure regulator and fine adjustment tap
2 Five feet of any type of rubber tubing interspersed with three filters, which connects the cylinder to
3 A rubber bung having two perforations
4 A length of glass tubing with an inverted thistle funnel at its lower end is passed through one perforation, and to its upper end is attached
5 The length of rubber tubing—(2 above)—passing to the oxygen cylinder
6 An L-shaped glass connexion passes through the second perforation and serves as an outlet for the oxygen A cotton wool filter is attached to its outer extremity

These pieces of apparatus (1—6) are required for aseptic stirring of the blood *If they are not available they may be dispensed with and occasional manual agitation substituted*

The bung is fitted into the mouth of a

7 Glass reservoir of 2 pint capacity [1]
8 A circular nickel gauze filter is placed at the bottom of the

[1] The two pint (1 000 cc) container is not so bulky as the more commonly used four pint size, and is for this reason in my opinion more practical

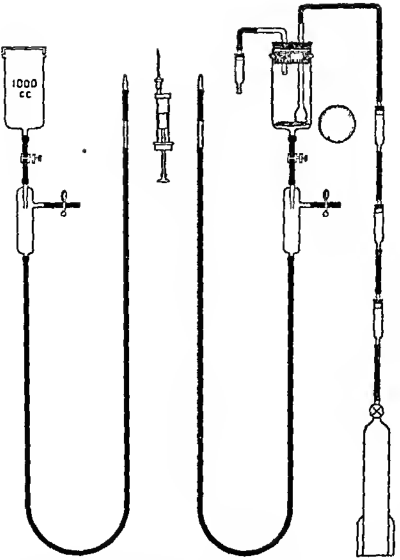


Fig 53 To show the adaptability of the simple gravity drip apparatus for large volume transfusion

Black—Apparatus common to both methods
Red—Additional apparatus required for large volume transfusions

reservoir, which serves to strain off any clots that may form The filter is made of pure nickel wire gauge 28, with 20 meshes to the inch

The reservoir is suspended by means of

9 The adjustable rod and frame illustrated in fig 46 or by some similar apparatus To the pointed lower end of the reservoir is attached

10 Four inches of soft rubber tubing (not pressure tubing), fitted with some form of adjustable screw clip The lower end of this is in turn connected to

11 A large glass drip bulb carrying a side arm to which is attached two inches of soft rubber tubing and a bull dog clip

The distal end of the glass dropper is joined by

12 Seven feet of *pressure* tubing to a

13 Glass cannula

The main difficulty met with in the management of a large volume transfusion is the maintenance of a constant drip rate Marriott and Kekwick say that they have overcome this objection by the use of a new pattern of speed regulator (p 251) My own more limited experiences with this drip regulator confirm their claims

Sterilization

All the items of apparatus except No 1 mentioned above require sterilizing and may conveniently be autoclaved together in a dressing tin, along with a gown ligatures and the instruments required in cutting down If the tubing is to be used on another occasion, it should be sterilized by boiling rather than autoclaving (see p 242)

TECHNIQUE OF LARGE VOLUME TRANSFUSION

A large volume transfusion is conveniently carried out in two stages

Stage 1

Selection of a vein
Erection of intravenous stand
Assembly of apparatus

Selection of the vein The transfusion starts by examining the patient for a suitable vein

Upper Limb The veins of the elbow region forearm, and back of the hand are examined

Forearm vein A forearm vein midway between the wrist and elbow and on the radial side is the one of choice This level is chosen as a cannula inserted here will not interfere with the movements of the wrist and elbow, which is more agreeable for the patient He thus has free use of his arm and nursing is greatly simplified—a matter of importance in a very ill patient —and at the same time the movement of the adjacent muscles promotes a better return of venous blood

Elbow vein On occasion it is more convenient to use one of

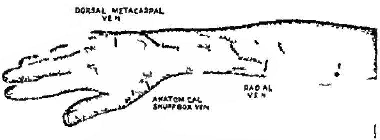


Fig. 64 Veins of the forearm and hand

the antecubital veins in spite of what has been said above in emergency transfusions in fat subjects and when it is anticipated that the transfusion will continue for more than 24 hours The forearm veins are generally small and tend therefore to thrombose earlier than those of the antecubital fossa For this reason if a long transfusion is contemplated interruption of the transfusion to change the vein may be avoided by choosing a large vein and a large cannula at the outset The veins of the elbow are however avoided in circumstances other than those first mentioned since insertion of a cannula at this level involves splinting of the limb to prevent flexion

Back of the hand If the forearm veins are not well marked the dorsal metacarpal veins should be examined There is often a well developed vein running across the anatomical snuff box and usually one or more on the back of the hand just proximal to the heads of the metacarpals

Lower limb The *internal saphenous vein* at the ankle In an individual in whom the forearm and hand veins are invisible

and in whom it may be desired to reserve the elbow veins for emergency transfusion or other intravenous therapy it is convenient to use the internal saphenous vein at the ankle This vein has the great advantage that its anatomical situation is absolutely constant and can therefore be relied upon when no other suitable vein can be found It also has the additional advantage of leaving the arms completely free

There are however two drawbacks in using this vein They are

1 In cases of shock or collapse the internal saphenous is not a satisfactory vein to use as the site of infusion is at the farthest point possible from the heart It has in fact been suggested that blood or other fluids injected at this level into a collapsed patient are lost in the peripheral venous circulation of the lower limb and pelvis In this way the fluid only reaches the heart after long delay

2 Thrombosis in these veins when used for large volume transfusion is earlier than when a vein of the upper limb is used This is probably due to the tendency to varicose change in these veins which is common to most individuals

Intravenous Stand (see p 239) As this is a gravity method some form of stand must be erected either at the top or bottom of the bed according to the vein selected This should be of such a height as to enable the reservoir to be suspended at least 3 feet above the level of the vein The greater the height of the reservoir the longer will be the column of blood and the more constant the flow

The operator now scrubs up and puts on a sterile gown

Assembly of apparatus The apparatus as seen in the diagram fig 53 is assembled in the order described on p 257 The reservoir is handed to an assistant who secures it in position and then adds warm saline to a depth of 2 inches The bung is then fitted The tubing is held up by the cannula at its extremity so as to form a U bend Saline is allowed to flow through until no more bubbles can be seen In this way all air is expelled The screw clip is adjusted so that a fast drip is running It should be stopped while running by attaching a 'bulldog' clip or artery forceps to the tubing about one foot away from the cannula

Stage 2

Venipuncture or Venesection

Venipuncture has two considerable advantages over venesection It is a much quicker technical procedure and it leaves the vein relatively undamaged a point of some importance if multiple transfusions are envisaged

It is indicated as the method of choice in those large volume transfusions which are not expected to take more than 8 hours that is to say in transfusions of 1 000 c c and less

A needle is however not quite so secure as a tied in cannula and venipuncture is therefore not advisable if the transfusion is being given at a distance from the operator s direct control if the transfusion is to be continued for a longer time as for instance in a bleeding patient or if the patient is restless or going to be moved during the transfusion

The 8 hour limit for the indwelling needle has been arrived at from a consideration of the following points

Venipuncture usually involves the use of the antecubital veins To ensure that the needle is not displaced during the transfusion it will generally be necessary to limit the movements of the limb by splinting with the forearm extended This position becomes very irksome after 8 hours If however there is a forearm vein of sufficient prominence for the venipuncture this should certainly be used and then the movements of the elbow will not require restricting Even so an indwelling needle begins to work loose after 8 hours As a result the needle may slip out and there is a tendency to leakage around the vein It must however be remembered that the majority of transfusions do not continue for longer than 8 hours

Venesection

Venesection will be necessary only in those cases in which venipuncture is not possible or is contra indicated because the patient is restless or the transfusion is designed to be one of long duration

Indications for venesection and tying in a cannula

1 Impalpable or invisible veins (usually fat subjects)
2 Collapsed veins

3 If the patient is restless

4 If the patient is to be moved during the transfusion

5 In cases of prolonged transfusion, e g more than 8 hours

6 If the transfusion is being set up and left to drip without trained supervision for example, at a distance from the operator's range of control

Technique of tying in a cannula

No excuse need be made for including a description of this simple procedure, since it is frequently performed indifferently, and nothing is less desirable in a very sick patient than prolonged fiddling over an operation which should be completed in a few minutes

The operation area.

If there is time it is an important advantage to give the selected area a thorough skin preparation with ether soap followed by spirit By doing this it will be found that the incidence of wound sepsis will be considerably diminished In the case of the foot a thorough toilet from the toes to the knee should be made

The *line of the vein* is made to stand out clearly before infiltrating with local anaesthesia, and marked with a blue skin pencil It quite often happens that after infiltration the vein collapses and its exact course is forgotten It is generally undesirable to maintain the use of a blood pressure apparatus for this purpose throughout the operation as it becomes uncomfortable for the patient

The operation area should now be isolated with *sterile* towels

A local *anaesthetic* is given intradermally at first, and then subcutaneously

*The incision should be **transverse** unless the line of the* vein was clearly visible before starting, in which case a parallel incision will give a better exposure When the exact position of the vein is uncertain a transverse incision gives a much better chance of locating one, and has the advantage that it can be enlarged half way round the limb if necessary A small incision is practical only if the line of the vein is prominent,

if the case is not one of urgency, and if the operator has had considerable experience of previous venesection

Forearm and hand The three most reliable veins are the dorso metacarpal vein, anatomical snuff box vein, and radial vein in the forearm

The exact technical details to be followed for the insertion of a cannula into a vein are illustrated below

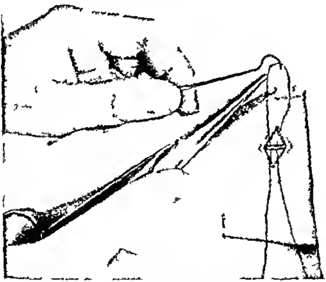
Procedure

FIG 75

(i) A liberal transverse incision is made and the vein exposed by means of two non toothed dissecting forceps and cleared of underlying fascia

IG 56

(ii) A small aneurysm needle is passed under the vein and threaded with a loop of plain catgut



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(iii) The loop of catgut is drawn under the vein and divided with scissors This leaves two strands of catgut behind the vein This manœuvre avoids passing the aneurysm needle twice.

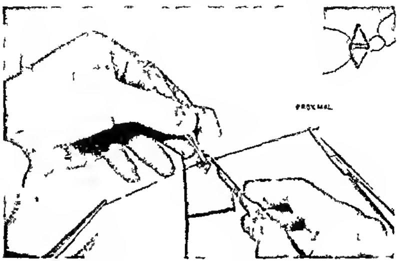

Fig 58

(iv) *Proximal strand* This is loosely tied in a single hitch and the two ends secured in artery forceps

Distal strand The vein is ligatured at its most distal point and the ends of the tied catgut are secured in artery forceps This arrests the flow of blood from below

The two catgut slings are now made taut and the vein is lifted out of the wound The lower catgut sling can be conveniently held by the operator himself, and the upper sling —if no assistant is available—can be made taut by attaching the forceps to the towel With a sharp and small scalpel not scissors a transverse nick is made in the anterior wall of the vein close to the lower catgut sling A scalpel is easier to manipulate than scissors When opening a small vein there is a danger of dividing it completely across if scissors are used

Unless the opening in the vein is made near its distal end, the upper edge of the skin wound, by overlying the opening into the vein makes the manœuvring of the cannula into the lumen more difficult

To confirm that the lumen of the vein has been entered loosen the upper catgut sling and reflux of blood will occur

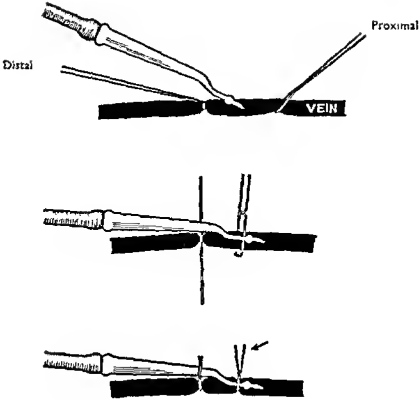

Fig 59

(v) To insert the cannula, the edge of the opening into the vein is picked up with fine dissecting forceps, and the cannula, held in the other hand, is introduced into the vein

The single hitch on the upper sling is now tightened behind the bulbous extremity of the cannula the knot is completed and the ends left *long* (arrow) to facilitate removal of the cannula at the end of the transfusion (Fig 59)

The long ends of the distal ligature are tied round the shaft of the cannula further to secure it in position

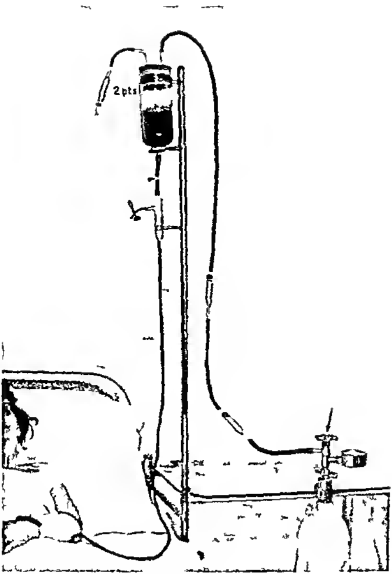

FIG. 66. *A large volume transfusion in progress.* The dotted rectangular area indicates the position of the drip regulator—when this is used. The arrow is pointing at the fine adjustment tap of the oxygen pressure gauge. The method of suspension illustrated here by multiple screw-on rings is not recommended (see fig. 53). Not more than one donor's blood at a time should be placed in the container. This lessens the risk of sub-group reactions and gives an opportunity for washing through with saline at regular intervals.

The fluid in the tubing should now be allowed to flow through the cannula to make sure there is no obstruction

The skin edges are approximated with fine silkworm gut, and one stitch incompletely tied is inserted over the line of the cannula to close the wound when it is withdrawn

It is usually advisable to place a small gauze swab behind the junction of cannula and tubing to raise the hilt of the cannula so that its point lies comfortably in the vein and not directed up against the anterior wall

The rubber *tubing close to the* cannula *is strapped to the* skin *with two pieces of adhesive tape* This maintains the position of the cannula and will allow any unexpected tug upon the tubing to be transmitted to the skin rather than to the cannula

The cannula and adjacent rubber tubing are covered with gauze and a thin layer of wool and then bandaged in position care being taken not to bandage tightly above the level of entrance of the cannula so that the entering blood will not be obstructed

A loop of the tubing should be included in the bandage for two reasons (i) to provide slack in case of any sudden strain (ii) *to raise the temperature of the incoming blood from room to body temperature by its contact with the skin over the last* 18 inches

The insertion of the cannula is not infrequently made while the patient is unconscious either in the theatre or while the patient is coming round after an operation In these cases it is advisable to prevent movements of the limb by splinting for the first few hours

MANAGEMENT OF THE TRANSFUSION

Maintaining a constant drip rate

Blood introduced at a rate of 40 drops a minute will usually run for several hours without requiring any readjustment of the screw clip provided the reservoir is *at least* 3 feet above the level of the vein (Note above the *vein*, not the bed or the floor)

A nurse should constantly *inspect the drip feed* and it is my own practice to leave instructions that the blood should be made

to run in a continuous stream for a moment or two *once every hour* This seems to clear the cannula of any commencing clot formation A small amount of normal saline should be added to the container before each addition of blood with the purpose of flushing the tubing

If the drip rate slows early in the course of the transfusion the *screw clip should be readjusted*, and the effect observed

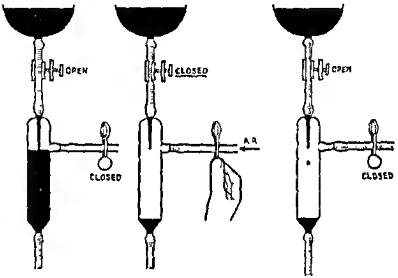

FIG 61

If this manœuvre does not restore an even flow there is an obstruction somewhere This is sometimes due to *tight bandaging* or to the weight of the bedclothes on the limb above the point of entry of the cannula, to *malposition of the needle* or *cannula* in the vein or to the use of collapsible rubber tubing which has become kinked or the patient has overlain

If the drip rate stops it is probably due to clotting in the cannula or it is because the cannula has come out of the vein

Clotting in the cannula.

Clotting in the point of the cannula will occur if the drip is allowed to stop—even momentarily Provided the drip has not been stopped for more than five minutes, it will be safe to try to

displace the tiny clot present by compressing the tubing two or three times between the finger and thumb close to the patient s arm If this fails 5 c c of sterile normal saline should be injected sharply through the tubing close to the cannula after obstructing the tubing above the site of injection with an artery forceps

Displacement of the cannula

Displacement of the cannula rarely occurs if the pattern recommended is used and secured as suggested and if in addition the limb is immobilized if the patient is unconscious or restless

Creeping up of blood in the drip bulb

After several hours the level of blood in the drip bulb tends to rise and if this is allowed to continue the end of the dropper will become covered with froth The side arm of the drip bulb is there to deal with this The main regulator screw clip should be closed and the side arm clip opened for a moment or two till the blood level has fallen under atmospheric pressure to the bottom of the drip bulb There is no risk of air embolism in this manœuvre or even if the side arm clip comes off unnoticed in the course of the transfusion (Fig 61)

Phlebitis

Some degree of phlebitis usually appears in 12 to 24 hours Its onset is earlier in the lower limbs than when a forearm vein is used possibly due to the greater tendency to pathological change of a varicose nature in the saphenous system

The patient complains of pain which is accentuated by increasing the drip rate and there is redness and tenderness over the vein which slowly spreads up the arm or leg The temperature rises and there may be severe constitutional disturbance if the cannula is not changed I have had experience of one large volume transfusion with extensive phlebitis in which the ensuing general reaction associated with hyperpyrexia was directly responsible for the patient s death

With the first appearance of phlebitis the cannula should be changed to a vein in another limb

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CHAPTER XVIII

TRANSFUSION IN INFANTS

Some of the most dramatic results in medicine are to be seen following the transfusion of blood to small infants In the past the tendency has been to withhold transfusion in many instances in which we now know that the intravenous introduction of blood will produce a cure—even though we do not know exactly how the blood brings about its good effect

The conditions for which transfusion is particularly valuable are the haemorrhagic diatheses which include the haemorrhagic diseases of the new born and the haemolytic anaemias of the new born and early childhood Transfusion may also be required in the acute intestinal disturbances of infancy at certain circumstances The technical and other details discussed in this chapter refer to infants and not to older children

THE BLOOD-PICTURE AT BIRTH

As the blood picture at birth differs very considerably from that occurring in the adult, and as a knowledge of it is necessary for the accurate determination of dosage in the various diseases affecting the blood at this early age, the normal variations will be enumerated

THE NORMAL INFANT AT BIRTH

The red corpuscles

1 The average *number* of red cells is 7 000 000 per c.mm the normal range is from 6 500 000 to 7 250,000 By the twelfth day the count has reached normal adult levels

2 *Nucleated red cells* mostly in the form of normoblasts, form a definite proportion of these cells and are present in the proportion of 500 to 1 000 per million red corpuscles The number of circulating normoblasts is reduced by half by the end of the first week

3 *Reticulocytes* form 10–20 per cent of the red corpuscles at birth but are reduced to within normal limits—1 per cent —by the end of the first week

4 The *size* of the corpuscles the average diameter is high—8 4 μ After birth, the cells gradually become smaller, but do not reduce to the adult diameter of 7 2 μ until the end of the first year

The haemoglobin

The haemoglobin averages 145 per cent (Haldane) or 20 grammes per cent at birth During the first three months of life there is a sharp fall from the high birth value to 75 per cent This figure rises again to 90 per cent by the end of the first year

The leucocytes

At birth there is a high leucocyte count approximately 18 000 white cells per c mm and these are predominantly polymorphonuclear

During the first two days of life the count falls to about 14 000 but rises again to reach 17,000 per c m by the twelfth day, the predominant cell now being the lymphocyte

During the next twelve years the leucocyte count gradually falls to reach the adult level of 6 000 per c mm

It is useful to remember that at the age of 4 years there are approximately 4 000 per c mm of both polymorphs and lymphocytes and that the percentage of each is about 40 (Whitby and Britton 1937)

The platelets

The blood platelets are present at birth in the same proportion as in the adult that is 400 000 per c mm

The fragility of the red cells

This is normal

Coagulation time

The coagulation time is the time taken for shed blood to clot

This is prolonged in infants at birth It is maximal on the second day and normal in ten days

The normal coagulation time as estimated by the capillary tube method of Wright is particularly influenced by temperature The readings differ widely depending on whether the test has been made at room (22° C) or body (37° C) temperature An individual having a normal coagulation time should always be used as a control

Normal times for an infant are

Temp	*Normal adult*	*Normal infant (during first week)*
°C	Mins	Mins
22	10–15	12–21
37	5–10	6–12

Bleeding time

The bleeding time is the time taken for a superficial needle wound to stop bleeding This is normal and is 2–5 minutes

The blood group.

An infant at birth has a fixed blood group This group remains unchanged in all circumstances throughout life

The isoagglutinins.

The isoagglutinins are fully developed at birth in a certain proportion of babies It is because of this possibility that a new-born infant must be given blood of a corresponding group, and for the same reason the direct test cannot be omitted (Kirwan Taylor, 1930)

Transitory agglutinins of the same type as the mother have been shown to be present at birth, which disappear within a few weeks but, as pointed out above, fully developed isoagglutinins differing from the maternal agglutinins may also be present at birth so that it is essential to use the same tests for infants as for adults

The isoagglutinogens

The agglutinogen factor is fully developed in the blood corpuscles at birth It is for this reason that the blood group of the new born babe can always be determined

THE PRINCIPLES OF DOSAGE

The principles upon which the dosage is determined are the same for infants as for adults In other words, in anaemic states the dosage is based upon the haemoglobin deficit, and in non anaemic states upon the amount of the particular deficiency of the blood which the transfusion is to supply

The Calculation of the Dosage

In anaemic states

In estimating the dosage in infants and children the principles already laid down when discussing transfusions in adults will still apply The only difference lies in their smaller size and proportionately smaller blood volume In a child this may be regarded as being equivalent to one eleventh of its body weight The administration of one tenth of the calculated blood volume in non bleeding cases produces a rise of 10 per

cent of haemoglobin as in adults An example will make this clearer

Weight in kilograms	Calculated blood volume—c.c.	Haemoglobin percentage before transfusion	Desired rise of haemoglobin	Estimated dosage
5½ (5 500 c.c.)	1/11 × 5 500 = 500 c.c.	0	40	500 × 40 / 100 = 200 c.c.

1 kilogram = 1 000 grammes = 1 000 c.c. fluid measure = 2.2 lb

In non anaemic states

In the absence of anaemia the dosage is most satisfactorily calculated from the body weight Infants under 12 months may safely be given 10 c.c. per pound of body weight or 20 c.c. per kilogram Thus a new born babe of 7 lb can safely receive 70 c.c. of blood intravenously

THE RATE OF INTRODUCTION

(a) Continuous drip transfusion

In relatively large volume transfusions for anaemia in children the haemoglobin as in adults should ideally be raised by 10 per cent four hourly In small babies this may mean a very slow rate In the example just cited the rate of introduction must have been 50 c.c. in four hours or 12.5 c.c. an hour or four drops a minute

(b) Short transfusions

In small volume transfusions the rate of infusion should not exceed 10 c.c. in five minutes Thus a transfusion of 100 c.c. should take not less than fifty minutes

Citrate or whole blood

Citrated blood should be used The dose of citrate as in adults is 0.3 gramme to 100 c.c. of blood

The use of whole blood in babies is particularly dangerous as the rate of introduction must necessarily be much too fast in order to avoid clotting Furthermore there is no evidence that the results obtained differ in any way from those obtained when using citrate even in the haemorrhagic diatheses

INDICATIONS

MELAENA NEONATORUM

and the other manifestations of the Haemorrhagic Diathesis of the new-born baby

In this account of the haemorrhagic diathesis of the new born which summarizes Capon's valuable contributions to the subject, I wish to lay stress upon *the prime importance of early blood tranfusion*

Out of the 61 cases reported by Capon (1937) the diathesis declared itself in 55 cases as a melaena and in rather less than half of these cases (21) there was associated haematemesis Rarely there may be bleeding from other mucous membranes, for instance those of the mouth nose vagina and urethra Haemorrhage sometimes occurs from the stump of the umbilical cord

The frequency in this series was in 1 in 405 live births, and females were affected slightly more commonly than males The average age of onset was 41½ hours after birth

In a number of cases ulcers or erosions have been demonstrated *post mortem* in the stomach and duodenum but it is not yet known whether these are usually primary or secondary to a submucous haemorrhage

Clinical features.

The onset which is usually about 36–48 hours after birth, may be sudden and dramatic as in the case of haemorrhage from a peptic ulcer in adult life These small babies withstand haemorrhage very badly

Differential diagnosis

In the differential diagnosis entero colitis will have to be considered, but in this condition there are no general symptoms In cases of swallowed maternal blood there will be diarrhoea and mucus Haemophilia will be excluded by familial and sex considerations, and there will be a history of a difficult labour in a case of birth injury

TREATMENT

General management.

The heart rate should be recorded hourly All blood lost must be carefully preserved, a loss of *more than 2 ounces being a*

severe haemorrhage in a new born babe Warmth should be supplied by bottles and an electric blanket and rest obtained by relieving the thirst with 5 per cent glucose in drachm doses by the mouth Rectal salines should not be given

Intramuscular injection and preparation for transfusion

Intramuscular injection

In the mildest cases an intramuscular injection should be given of 20 c c of untyped citrated blood obtained from the mother or father or any healthy available donor The blood can be citrated by adding 1 c c of 3 per cent sodium citrate to every 10 c c of blood (0 03 gramme of sodium citrate crystals) The injection should be made into the thigh and not the buttock—below the mid point and well away from the napkin area and so out of danger of infection If it is necessary to repeat the injection it should be made into the opposite thigh or deltoid region

Preparation for blood transfusion It is important that the intramuscular injection of blood *should only be regarded as a temporary measure* to be used while provisional arrangements are being made for a blood transfusion It is probably true to say that cases which recover with intramuscular injections of blood would probably recover without them and that patients who die following intramuscular injections only would probably have recovered if they had been given a blood transfusion

The preparations include

1 Group the baby and the donor

2 Collect serum from the baby for cross matching

3 Obtain some one experienced in this work to perform the transfusion

4 Examine the patient for a suitable vein on the scalp or at the ankle

Intravenous transfusion

If the child becomes restless or if the bleeding continues or starts again or the pallor increases within the next two hours no time should be lost in giving a blood transfusion of 60–100 c c of citrated compatible blood A second intramuscular

injection of 20 c c should be given if there is delay in obtaining a suitable donor for transfusion

Post-transfusional care. *Feeding* The infant should return to the breast as soon as the bleeding has ceased There is no need, nor is it right, to withhold fluids, as hunger will cause peristalsis

Repair of the anaemia An anaemic infant is very prone to infection Two or three days after the bleeding has stopped the degree of anaemia should be re determined and a transfusion given if this is of more than moderate degree

ERYTHROBLASTOSIS FOETALIS

There are two varieties of this haemolytic anaemia of the new born

1 Icterus gravis neonatorum in which severe anaemia is associated with jaundice and

2 Anaemia haemolytica neonatorum in which there is a severe anaemia of the same type but without jaundice

ICTERUS GRAVIS NEONATORUM

In icterus gravis neonatorum the jaundice may be so deep that the underlying anaemia is masked unless the condition is suspected and confirmed by a blood count

Clinical features

At the birth of the child it may be noticed that

(*a*) The vernix caseosa is golden yellow
(*b*) The placenta is unusually large
(*c*) There is oedema of the limbs
(*d*) The infant is jaundiced

Development of jaundice is early It is present in about half the cases at birth and in the remainder with rare exceptions it develops on the second or third day The jaundice is marked and rapidly deepens On examination of the abdomen the liver and spleen will be found to be palpably enlarged

The diagnosis is decided by the blood picture which is one of destruction and regeneration proceeding side by side An example of the blood picture is as follows

Haemoglobin	30 per cent
Red blood corpuscles	1½–2½ million
Amongst these are many *nucleated* red cells which are made up of erythroblasts megaloblasts and normoblasts the normoblasts being present in the proportion of about 12 to 1 of the less mature nucleated red cells	10 000–30 000
Reticulocytes	10 per cent
White blood corpuscles	35 000 (chiefly granulocytes with a few immature cells of the granulocyte series)

TREATMENT

Except in the mildest cases in which a spontaneous recovery is likely it is generally agreed (Hawksley and Lightwood 1934) that intravenous transfusion of blood holds out the best hope of a cure Unfortunately there is a tendency to withhold this valuable remedy until the anaemia is too grave for any therapeutic measure to be successful The authorities mentioned above recommend that *repeated transfusions should be given* of 60–100 c c depending upon the weight of the child until the haemoglobin level is restored to within the lower limits of normality Four or more such small transfusions may be required and *they should be given at intervals of four days to a week* (see alternative in next paragraph)

Large volume transfusion By the time the fourth or fifth transfusion is due there may be some difficulty in finding a suitable vein This may prove rather a serious obstacle in a very ill child and for this reason it is an advantage to reduce the number of transfusions by giving the blood in one or possibly *two larger volume drip transfusions*

Prognosis

Unless the diagnosis is made early in the disease and appropriate treatment started the prognosis is bad and is said to be associated with an 80 per cent mortality In the cases which recover a residual spasticity together with mental deficiency may remain This is said to be due to jaundice of the nuclear masses of the brain (kernicterus) which produces degeneration of these areas of the nervous system

SUMMER DIARRHOEAS

The collective phrase 'summer diarrhoeas' is a comprehensive term and includes examples of diarrhoea and vomiting of widely different aetiology In some there is a specific infection of the intestinal tract such as occurs in food poisoning in typhoid, dysentery and salmonella infections but apart from these there is a large group of cases in which no specific infection of the intestinal tract can be found and of this group the largest number are due to a parenteral focus of infection elsewhere in the body particularly otitis media In a certain few no obvious infection seems to be present and one has to think of these as being environmental and due to great heat with high humidity

Whatever their aetiology the diarrhoeas produce a common clinical picture—that is dehydration and wasting In certain circumstances as will be discussed later blood transfusion may be very valuable It is as well to emphasize at the outset however that the routine use of blood transfusion for diarrhoea and vomiting is by no means without danger

Diarrhoea complicated by DEHYDRATION only

In an untreated case of diarrhoea there comes a time when the intake of fluid does not adequately balance the fluid loss To maintain the blood volume the tissues are drawn upon and the child becomes dehydrated Clinically this is shown by a dry inelastic skin dryness of the mouth sunken eyes and fontanelle and those signs which depend on circulatory failure namely cold and cyanosed extremities a feeble pulse and diminished urinary excretion

At this stage blood transfusion is contra indicated because the fluid requirements can be equally well restored by means of water glucose, and saline Aldridge of Birmingham, in a personal communication (1938) says

> In the treatment of dehydration in infants we have come to the conclusion that blood transfusion is not only of very little therapeutic value but may also be of harm to the recipient as the degree of concentration of the blood may be increased as the result of transfusion In assessing the extent of haemoconcentration we have done red cell counts haemoglobin estimations and also haematocrit readings on all

specimens and have found that they are almost invariably increased in those cases which are dehydrated clinically However, as some of the children have quite a marked degree of nutritional anaemia, part of the increase of red cells may be the result of this In cases of this type we have found that the haematocrit readings are of most use in determining the degree of concentration of the blood Also it seems that cases with a blood count of over 6 000 000 per c mm will stand a transfusion quite well as long as the haematocrit reading is not unduly high i e is under 40 per cent'

A similar attitude is adopted in Liverpool where Forshall says in a personal communication (1938)

'Cases of summer diarrhoea are being treated by continuous intra venous Hartmann s solution with glucose which is kept running until the diarrhoea stops We have only used transfusion to correct anaemia following the acute condition

My own experiences at the Royal Waterloo Hospital are in agreement with these observations

Diarrhoea complicated by MALNUTRITION as well as by DEHYDRATION

If diarrhoea and vomiting continues malnutrition is likely to develop from deficient absorption of protein If the child is seen for the first time in this stage—that is to say with dehydrated tissues and commencing malnutrition—*it is important to relieve the dehydration first,* before dealing with the malnutrition This is because, although the total serum proteins are depleted the serum protein level is high owing to the diminished volume of fluid in the circulation

The effect of a blood transfusion at this stage will be further to raise the serum protein level and hence the osmotic tension Clinically, this will be seen as an increase in the existing dehy dration In other words a *blood transfusion at this stage will merely aggravate the condition* already present

Treatment

In cases of dehydration with malnutrition the treatment should be carried out in two stages,

1 *Relief of dehydration* The lost fluid should first be replaced by adequate hydration by intravenous or other routes This will dilute the serum proteins to normal or below If a hypopro teinaemia is produced the tissues may even become oedematous

2 *Restoration of serum protein level* Now is the time—when the dehydration has been relieved—to raise the serum proteins by transfusion and so relieve the malnutrition

The dosage

Malnutrition and anaemia often go hand in hand so that a haemoglobin estimation although not an exact calculation of the degree of malnutrition will give a useful lead as to the volume of blood which should be transfused

PYLORIC STENOSIS

In pyloric stenosis there is a triple lesion There is dehydration from loss of fluid in the vomit there is alkalosis from loss of chlorides in the same way and there is hypoproteinaemia from inability to absorb protein

Treatment

The *dehydration* must be dealt with *first* by the administration of glucose and saline (see p 282)

For the *hypoproteinaemia* blood transfusion is indicated and this is particularly important because of the coexisting alkalosis a state in which the tissues are also hydrophilic The object of a blood transfusion is purely to raise the serum protein and so increase the osmotic pressure of the blood By so doing the hydrophilic tendency of the tissues will be counteracted which a simple infusion of saline cannot achieve At the same time by increasing the circulation through the kidneys excess of alkali will be excreted and the acid base balance restored

The transfusion should be given on the day before operation The dosage of blood will be determined by the weight of the infant Improvement will be shown by a return of tissue turgor an increased excretion of urine a pulse of better volume and by the return of chlorides to the urine

The DYSHAEMOPOIETIC ANAEMIAS of Infancy and Early Childhood

The dyshaemopoietic anaemias are associated with inefficient blood production They are most commonly due to deficiency of iron in the diet or to infection less commonly to vitamin or endocrine deficiency

The treatment of these anaemias is the treatment of the cause, and as they respond quickly and well, the need for blood transfusion is exceptional and as a routine measure unnecessary. The commoner types of anaemia may be enumerated so that the reader, being on the watch for them, will be able to elucidate the cause and remedy the deficiency in its simplest way.

The iron deficiency anaemias

The anaemia of *prematurity* is the earliest example of an iron deficiency anaemia seen and is due to the fact that approximately two thirds of the iron reserve of the foetus is laid down in the last three months of pregnancy. Thus the infant is born before it has received its full quota of maternal iron. The anaemia of *multiple births* is well known and is due to the maternal supply of iron being insufficient for more than one infant. After the third month of life a *nutritional* anaemia may develop, due to deficient iron in the mother's milk, and a similar anaemia occurs from excessive *prolongation* of *milk feeding*, the supply of available iron being insufficient for the rapidly growing child. Most of the above anaemias are due to deficient ingestion of iron, but anaemia may also develop from deficient absorption. This is seen in *coeliac disease*.

The anaemia of infection.

Septic foci such as discharging ears, tonsillitis, and so forth are always potential causes of anaemia. If the infection is eradicated the child will usually respond rapidly to an iron-containing diet. Where infection appears to be the cause of the anaemia, but cannot be treated, one or more small transfusions afford the best method of treatment since the blood will not make any attempt to regenerate until the infection has disappeared. In many of these infants, particularly those who are failing to gain weight, a small transfusion will cause a sudden change for the better in the patient's condition which frequently marks the beginning of a steady and lasting improvement.

Endocrine and vitamin deficiency anaemias.

The anaemia of cretinism responds well to thyroxin and the anaemia of scurvy to vitamin C, although the latter is not so simple to treat as in adults as it is often associated with infection.

Nutritional anaemias

In the nutritional anaemias of early childhood transfusion is necessary only in cases in which the cell volume and haemoglobin content are nearing the level which is incompatible with life. In these circumstances one or more transfusions will frequently remove the patient from the danger zone until a proper diet will gradually raise the cell volume and haemoglobin content to normal levels.

Statistics

It is interesting to compare the number of blood transfusions given during the same year (1937) at two well known hospitals of much the same size (Toronto Hospital for Sick Children 320 beds, Great Ormond Street London 257 beds increased to 326 beds in 1930). Very many more transfusions were given in Toronto than in London. The difference is partly due to the greater incidence of gastro-enteritis in Toronto but mainly due to a different attitude of mind in regard to the value of transfusion as a therapeutic measure in this disease.

1937	*Toronto*	*London*
Total number of transfusions	1 186	[illegible]
Number under 1 year	445	67
Number over 1 year	741	72
Number whole blood transfusions	[illegible]	0
Number citrate transfusions	37	[illegible]

Indications

Gastro-enteritis is the commonest indication in both Hospitals but apparently the incidence in Toronto is very much higher than in London. At Great Ormond Street out of approximately 75 admissions for gastro-enteritis 30 received transfusion, i.e. under 50 per cent. The Toronto report says "In summer diarrhoea blood grouping is a routine in the admitting room and except in the very mild cases transfusions are routinely given as soon as the patient reaches the ward."

Figures very similar to the London statistics come from the Hospital for Sick Children, Glasgow. Fleming in a personal communication says "During the two years January 1936 till

December 1937 in my unit of 80 beds, 58 children were transfused, the total number of transfusions being 133. Fifty of the children were under 1 year of age and 8 over 1 year. There were 5 cases of haemorrhagic disease of the newborn—all recovered—and 9 of icterus gravis neonatorum, of whom 4 recovered. Citrated blood was used in all cases.'

THE TECHNIQUE

Although the apparatus used when transfusing infants is essentially the same as that standardized for adults there are certain important changes in procedure required These changes include

1 The choice of vein
2 The technique of entering the vein
3 The use of positive pressure to make the injection

The choice of vein (up to 12 months)

(i) It is wise to choose a vein in which subsequent thrombosis can do no harm For this reason transfusion of blood via the superior longitudinal sinus should never be performed It is occasionally justifiable to withdraw blood through the anterior fontanelle but never to inject it A large enough number of instances of sinus thrombosis and subdural or subarachnoid haemorrhage with hemiplegia have now been reported for us to say that the sinus approach is highly dangerous Fortunately there are other routes at our disposal

(ii) When possible the transfusion should be given without cutting down upon the veins In a baby multiple transfusions or other forms of intravenous therapy are more commonly given than in adults so that it is important to avoid cutting down for as long as possible as the number of veins suitable for venesection purposes is very few

The method of entry

By venipuncture In an infant the superficial veins particularly of the *scalp* are more easily seen than the median cubital and basilic at the *elbow* For most purposes the superficial temporal or frontal scalp veins are the most satisfactory but any visible vein may be used Sometimes the *external jugular* vein is prominent but its movements are rather more difficult to control and the position of the head turned to the side is awkward when it comes to making the injection Other veins that should be looked for are the *dorsal metacarpal* veins and there is sometimes a fairly well marked vein to be found on the radial side of the *index finger* Occasionally there is a dorsal

cutaneous vein on *the foot* into which a needle can be inserted If all other routes fail the *common femoral vein* may be used

By venesection The only constant veins which can be

FIG 62 Immobilizing the lower limb of an infant
(*a*) The strapping is first fixed to the *back* of the splint
The black line indicates the site and direction of the incision to expose the internal saphenous vein as it passes in front of the medial malleolus

relied upon for venesection are the external jugular vein in the neck the antecubital veins at the elbow, and the internal saphenous at the ankle

If possible the external jugular veins should be avoided, as exposure of these is liable to leave an unsightly scar *The vein*

of choice is the internal saphenous at the ankle where it runs anterior and slightly external to the internal malleolus One may depend on finding this vein even in the tiniest babies It should be exposed by a transverse incision (see fig 62)

Fig 63 Immobilizing the lower limb
(*b*) The strapping carried across the foot which is fixed in the abducted position

Difficult cases If the saphenous cubital and jugular veins have been used and there is no superficial vein visible an injection into the common femoral vein or into the peritoneal cavity is to be preferred to injection into the superior longitudinal sinus In desperate cases Tzanck has made successful intracardiac transfusions (Tzanck 1927)

TRANSFUSION WITH SYRINGE AND TWO-WAY TAP

The apparatus.

The apparatus required is the same as that already described as being used in the tube and funnel type of gravity transfusion in which entry into the vein is made by record syringe and two-way tap (p 206), but with one addition—another 5 c c syringe and two way tap are needed This syringe is connected by the tap to the tubing half way between the reservoir and needle It is used by an assistant to make the injection once the vein has been entered by the operator It is required for two reasons owing to the small size of the veins a needle of very fine calibre has to be employed, and this will not allow a gravity flow—hence some way of making positive pressure has to be found The other reason for using this syringe is to enable the operator to concentrate on maintaining the immobility of the needle, the position of which is prejudiced should the attached syringe be used instead, for making the injection The needle used should be 22 gauge and 1½ inches in length

Preparation of the infant.

If a scalp vein is selected, the surrounding hair must first be shaved away Shaving will often make almost invisible veins stand out

The struggles of the baby must be restrained by

(a) Sedatives before the transfusion

(b) Skilful blanketing so that neither the arms nor legs are free

(c) Firm control of the head by an assistant while the injection is being made

The injection.

1 The glass container, tubing, and both syringes are filled with warm saline The needle is fixed to the distal or operator's syringe It should be put in connexion with the syringe by turning the tap in the appropriate direction

2 The vein (superficial temporal) should be made prominent by the assistant pressing on it with his thumb just above and

in front of the ear If this does not make the vein stand out, the child should be forced to cry Further distension may usually be obtained by tapping over it with the finger for a few moments' (Schwentker 1931)

3 The technique of injection is exactly opposite to that employed in the adult *The procedure is as follows* The syringe is held in the right hand in such a way that the tip of the index finger overlies the hilt of the needle The needle is pushed through the skin to one side of the vein to avoid pricking it prematurely The venepuncture should now be attempted Schwentker advises that the vein should be entered from its deep aspect As soon as one feels that the point of the needle has entered the lumen a *trial injection* is made In these small veins it is useless to attempt to withdraw blood the vein wall simply collapses If a small swelling appears this should be massaged away and another attempt made As soon as the vein has been entered the operator should slide his index finger along the shaft of the needle until it overlies its point of entrance through the scalp The *finger* should be kept in this position without moving throughout the injection The injection can now be made with safety preferably by the assistant using the second syringe but if this is not available by the operator with his free left hand

TRANSFUSION WITH THE ROTARY PUMP

The syringe method of transfusion described has the disadvantage that the plunger of the syringe used by the assistant for making the injection tends to stick in the barrel after a short time This is due to the very slow rate of injection which is necessary If a rotary pump is available it is more convenient to use this in place of the assistant s syringe as a more regular and easier flow will be obtained The pump can be placed in the circuit before or after the vein has been entered The actual venepuncture must be made with a syringe which should be held in position throughout the transfusion as in the previous method

Transfusion with multiple syringes (Whole Blood) (see p 105)

Gravity method of transfusion—in infants and older children

The transfusion can be given by the ordinary gravity method provided that a very fine needle is not being used—a point which is determined by the size of the patient's veins In infants it is unusual to be able to give blood by a gravity method except possibly when a cannula can be tied in In older children, on the other hand, the technique is of course the same as for adults

Transfusion with large syringes

Owing to the relatively small amount of blood required for transfusion in infants it has been suggested that the total amount to be injected could most conveniently be collected into a large syringe containing citrate and from this directly injected into the child This method in practice involves the use of heavy and bulky syringes which are unwieldy to manipulate and difficult to control with accuracy and is not advised

LARGE VOLUME DRIP TRANSFUSION

The principles of the large volume drip transfusion as described for adults may be applied unaltered for infants and children The only difference lies in the smaller size of the patient, so that the amount of blood and rate of introduction will be proportionately reduced and the apparatus though the same, can conveniently be smaller

Variations in apparatus and procedure

(i) The reduction in volume of blood to be transfused allows a smaller reservoir to be used

(ii) The reduction in rate is obtained by adjustment of the special capillary tube regulator described elsewhere

(iii) The small size of the veins makes it necessary to cut down and use a very fine cannula The ordinary type of glass cannula cannot be drawn out into a very fine point consistent with strength Kekwick recommends a metal cannula of the type used in experimental physiology, and Brush (1932) has found a ureteric catheter very satisfactory

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CHAPTER XIX

AUTO TRANSFUSION

SUCCESSFUL instances of blood replacement are in the experience of every surgeon Large series of cases have been reported by Newton (1933) and Stabler (1934) in Great Britain by Tiber (1934) and Watson and Watson (1936) in America

The reinfusion of blood shed into the peritoneal cavity was first practised by Thies of Leipzig in 1914 but as early as 1885 John Duncan of the Royal Infirmary Edinburgh reinfused the blood which dripped from an amputated limb after adding sodium phosphate as an anticoagulant

Blood replacement is most commonly practised in cases of haemorrhage into one of the body cavities sometimes the pleura more often the peritoneal cavity By far the commonest association is with the intraperitoneal rupture of an ectopic pregnancy although reinfusion may also be practised following the rupture of a liver or spleen It may even occasionally be worth while to exsanguinate a viscus after its removal for instance following the removal of an enlarged spleen particularly if the splenomegaly was associated with anaemia

The risks involved

Tiber (1934) reported 189 cases of ruptured ectopic pregnancy which received auto transfusion There were three deaths and six severe reactions of a haemolytic type directly attributable to the transfusion In each of the fatal cases the blood had been in the peritoneal cavity for *more than 72 hours* Coley (1928) also reports a severe haemolytic reaction—again after infusing blood more than three days old Grossmann (1924) records a fatal haemolytic reaction following the reinfusion of blood coming from a ruptured liver In these circumstances the blood may become mixed with *bile salts* which are well known haemolytic agents

Other severe reactions have been explained by the use of blood which has become *infected* either by direct contamination from a coincident bowel perforation or following permeation from the bowel in cases of long standing rupture

In other cases the reaction appears to be due to the introduction of *toxins* formed from decomposing blood clot

Ricci and di Palma (1934) have shown that the red cell count is microscopically normal up to 72 hours after perforation

The risks associated with reinfusion of blood would appear to be in the main avoidable by careful selection of cases

Thus blood replacement should not be attempted

1 If the intraperitoneal haemorrhage is of more than 24 hours standing
2 If there is an associated bowel or other hollow viscus injury
3 If the biliary apparatus has been damaged

The advantages of auto transfusion are considerable for the *delay* is avoided that would be spent in grouping a patient, obtaining a donor cross grouping and collecting the blood Furthermore the *risk* of an incompatible transfusion or the transmission of disease is eliminated—although severe reactions may occur if old or contaminated blood is used

Procedure

The general procedure to be adopted in a case of intraperitoneal or intrathoracic haemorrhage in which transfusion will be necessary should be as follows

A *donor* of the same blood group should be obtained and cross matched with the patient before the operation and he should attend at the time of the operation in an adjacent room The presence of the donor is necessary in case the shed blood is found to be unsuitable because of clot formation or contamination or because of technical difficulties associated with its collection or administration As a rule there is plenty of time to carry out this precautionary measure

It has been my experience that there is a tendency for the patient to collapse comparatively early in the operation for the removal of a tubal pregnancy that is towards the end of the manipulations to deliver the blood In point of time this is before the extra uterine gestation has been removed and before the collected blood is quite ready to be reinfused For this reason in all these cases a slow *intravenous glucose saline* should be started as soon as the patient is on the table By being

prepared in this way, the reinfusion of blood can be begun at the earliest possible moment, and a less hurried transfusion performed

Technique.

The blood may be *collected* by suction or simply by baling it out by hand If suction is used only a small incision should be made at first so that blood is not lost by overflowing through the wound If the blood is being collected by hand a larger incision will be necessary from the first, and it will be found convenient to use a small boat shaped receptacle rather than a round container which is not so easily manipulated in and out of the wound Care must be taken not to allow water or antiseptic solutions to drip from the hands into the blood while this is going on

The blood is *received* into a sterile glass funnel lined with six or more thicknesses of gauze, muslin, or fine mesh silk, soaked in 3 per cent citrate The stem of the funnel is directed into the open mouth of the container selected to receive the blood This reservoir should contain at least 50 c c of 3 per cent *sodium citrate, which should be added before the operation* begins The funnel and container are held in readiness by an assistant standing in an accessible position on the opposite side of the table to the surgeon

There is no need to keep the blood warm while it is being collected—this only complicates the procedure It can readily be raised to body temperature before infusion

The reinfusion of the blood can now be started by any method familiar to the transfuser and available in the operating theatre

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CHAPTER XX

STORED BLOOD

GENERAL CONSIDERATIONS

AND that there may be blood throughout all the land of Egypt both in vessels of wood and in vessels of stone

In Russia all the large hospitals use stored blood almost to the exclusion of freshly drawn blood and the professional donors simply attend a Central Institute for its collection The feeling in England is that this is carrying change too far Where voluntary services predominate the wholesale diversion of a donor s services to a common supply might very well dry up the springs of altruism In France Spain and the Americas preserved blood is also extensively used The question is whether there is any real need for hospitals to store blood I personally think there is so long as it is strictly limited to use in emergencies and it does not usurp the place of fresh blood on other occasions More often than not the occasion is an emergency only in so far as we are unprepared to give a transfusion or are asked to do so at the last minute I know of no other operation in which a little forethought can avoid so much confusion The preliminaries include routine *grouping on admission* of all cases which may require transfusion early *collection of serum* for the direct test and *centralization of transfusion equipment* which is sterilized and ready for use If a practice is also made of withdrawing *a pint of blood from a donor the night before* a major operation and if we can improve the *efficiency of our existing donor services* the occasions for using stored blood will be few and far between

Although the experimental work on animals shows that blood stored up to fourteen days is biologically active these results should be applied to transfusion in man with reservations The fragility of human red cells increases after four days of storage (Bagdassarov 1937) and although such blood might be transfused without actually haemolysing it is very doubtful whether it would exert any prolonged therapeutic effect Furthermore

as my own experiences have shown me, severe reactions may occur after injecting only forty eight hours old blood. In my opinion the period of storage should be limited rather than extended and should *in no circumstances be more than eight days*.

ORGANIZATION

The blood groups to be stored

Except in very large hospitals it will not be worth while to keep blood of all four groups. Individuals of groups AB and B make up less than 10 per cent of the total population, so that much wastage would occur if blood of these groups was stored as a routine. The remaining 90 per cent is almost equally divided between groups A and O (O being the so called universal donor). Opinion is divided whether both these or only group O should be stocked. In the present state of our knowledge it would probably be better to concentrate on a supply of blood of the universal donor group for the emergency circumstances with which stored blood is essentially concerned.

The source of donors for supplying blood for storage.

As to the sources of blood for storage purposes, there are three: the living donor, the placenta, and the cadaver.

The living donor may be a member of a transfusion service, a relative or friend of the patient, or the patient himself.

1 From members of a transfusion service. The conditions of service as they exist in the Soviet Republic will illustrate the chief points.

The donors are empanelled to form a professional service in very much the same way as in other countries, but instead of attending at a hospital when they receive a call they go to a central institute. There is one of these Blood Transfusion Institutes in each of the big cities of the Soviet, and a large number of smaller affiliated branches. As far as possible it is being arranged that these institutes shall be situated in or adjacent to a large hospital. In addition, a haematological department is being formed at each institute with its own laboratories and wards. In this way the clinical and experimental sides of haematology are being linked. Donors apply and go through the usual routine medical examination. In addition they are given a passport and their personal records are indexed at the office. The majority of the donors, unlike those in any other country, are *women*. In Leningrad in 1936 there was a total of

1,025 of which 1 094 were women Between them they yielded 1 000 litres of blood which was spread over 4 000 transfusions In many of the cases the blood was transported long distances to outlying country districts The occupations reported amongst the donors were as follows

Workmen and women	837
Nurses	244
Students	150
Trade apprentices	216
Married women with no salaried appointments	178
	1 625

Of these donors 29 served more than 30 times and 1 284 served more than 10 times

The donors are allowed 6 weeks between each service this limits them to a maximum of 8 donations a year

In England, where professional services are in a minority we have to look elsewhere for our supply of conserved blood

II From relatives and friends The use of relatives blood for purposes of conservation is much more satisfactory than for immediate transfusions If we wait for emergency circumstances to develop a band of excitable relatives may congregate time is spent in several groupings and unless a chance is taken with regard to syphilis there will be delay while waiting for the result of a test If transfusion is anticipated and the blood collected and stored in readiness much time and worry will be saved

III From the patient Occasionally an individual who has a full complement of haemoglobin and red cells has to undergo a major operation Unless he is anaemic the withdrawal of 400–500 c c will cause no ill effects and no grouping is required Although few patients can afford this contribution it is a source worth bearing in mind if a suitable donor is not at hand

IV. From other patients requiring therapeutic venesection Blood withdrawn for therapeutic reasons should always be taken into citrate by a closed method and put in the ice chest It will of course require grouping and testing in the usual way Suitable donors include cases of high blood pressure heart failure and perhaps polycythaemia vera The blood from the latter has a particularly high concentration of red cells and haemoglobin, and is said to give good results when transfused into patients with aplastic anaemia Polycythaemia is however, a disease of uncertain aetiology, so this blood should not be

transfused into healthy recipients—for example after haemorrhage from trauma For a further discussion on the use of polycythaemic blood see p 150 Blood drawn from patients with uraemia has also been used and is said to have no toxic effect upon the recipient

V From the paediatric department Mothers attending a paediatric department provided they are compatible can conveniently be used to make donations to their own infants Quite often, particularly in cases of diarrhoea and vomiting several transfusions are necessary at short intervals A single donation divided amongst several small containers will save the trouble of repeated venesection or demands upon a transfusion service

From the antenatal department It has been suggested that expectant mothers should give a pint of blood for storage any time after the seventh month by which time their blood counts have usually returned to normal In this way an obstetric department could be made independent of other sources of supply The individual contribution would not return to the donor but would be placed in a common pool from which she would have the right to draw when she subsequently entered hospital There are several objections to this plan In the first place it is doubtful whether the impersonal nature of the contribution would find favour with most of the mothers concerned In the second place *it is very questionable* whether non therapeutic venesection of a pregnant woman is wise, for if anything untoward occurred later on it might be difficult to absolve the antenatal loss of blood

The Blood Bank.

At the Cook County Hospital in Chicago a Blood Bank has been established and is working well Blood deposited in the bank from any of the above mentioned sources is credited to the service supplying it though the actual bottle of blood deposited will not necessarily be used by that service When the time comes for a transfusion the house officer applies to the 'bank cashier', that is to say the laboratory technician for blood of a specified group Provided the service or firm has blood of any group to its credit in the bank a bottle of the required group may be withdrawn a record of this being kept

The advantages of the bank are twofold

1 If a number of friends or relatives of unknown blood group offer themselves for transfusion, any one donor can be detained and bled, since the identical blood group is a matter of indifference, and blood is only being collected to maintain a credit balance at the bank In this way time is saved and confusion avoided If the patient requires blood before the grouping result is known this will be provided at the bank from some other source

2 Blood of the correct group can be obtained in exchange for blood of another group

At first sight it seems that some degree of deception must be practised in order to obtain blood for the bank A donor is told that a transfusion may be necessary for a relation in hospital and the blood is drawn and stored When the transfusion takes place, blood drawn from the bank, not necessarily that given by the particular donor, is employed This undoubtedly amounts to deception which could be avoided by explaining the facts to the donor Whether friends and relatives would then be as willing to part with their blood is another question The same problem arises when the blood is a self donation for example, in the case of a patient before operation or a woman attending the antenatal clinic There is no reason however why blood should not be obtained from these different sources and given to the patient for whom it was originally intended This practice would destroy the fundamental principle of the bank—the Exchange System—but would still have the other advantages associated with conserved blood

METHOD OF COLLECTION

There are two methods of collection practised at the principal centres using conserved blood the simple open method by means of a short length of tubing which empties into an open mouthed flask, and the common closed method of bleeding by creating a negative pressure in the collecting flask either by a rubber bulb or by mouth suction through an intervening filter

The open method.

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The open method.

Although it is true that blood is actually bactericidal to the ordinary organisms in the air of the average room, it is question-

able whether such a risk should be taken in the less bacterially pure air of a hospital If by any chance a fatal reaction followed the use of stored blood collected by an open method one s first inclination would be to question the sterility For these reasons the open method of collection should not be used if the blood is afterwards to be conserved

The closed method

It is my own practice when collecting blood for storage purposes to follow certain rules

(i) The blood is collected by a closed method
(ii) The container is autoclaved with the citrate *in situ*
(iii) The container is air tight when sealed
(iv) There is the shortest possible exposure of the contents of the container to the air
(v) The neck of the container is protected during collection and storage from dust collection so that the blood can be poured from it into another vessel with a minimal risk of contamination
(vi) The capacity is so arranged that 500 c c of blood and 50 c c of citrate almost fill the bottle thus ensuring a minimal volume of air in the container for contact with the upper surface of the blood

If a container with a greater capacity is used considerable wastage of blood may occur It would probably be an advantage to have in addition smaller bottles—of capacity 300 c c —to serve for the smaller transfusions

Description of the Container An entirely satisfactory container has not yet been devised Since I first wrote this section numerous different patterns of containers have been described (Elliott Biddle and Jorda 1939)

At present the most satisfactory in my opinion is the Macartney bottle already described on p 237 as a suitable standard container for ordinary transfusion work Such a bottle is readily supplied with a vacuum already present or negative pressure may be made by a rubber bulb or by the rotary pump as when collecting blood by the closed method (p 8) The mouth of the bottle can be stoppered with the standard aluminium cap or if preferred with a rubber cap which will allow

perforation It is an advantage if the container used for storing the blood can also be used for its administration This avoids duplication of apparatus and diminishes the risk of contamination

Mixed blood of the same group I am personally not yet convinced of the safety of mixing bloods of the same group, particularly those associated with sub groups because of the possibilities of sub group reactions Jorda (1939) holds the contrary view and says that the objections are purely theoretical and not confirmed in practice He says that mixture of bloods of the same group gives the following advantage

First, a very homogeneous blood (biologically speaking) is obtained, with a normal quantity of cells, haemoglobin, glucose, urea, and other constituents and the product of the mixture of several bloods tends to approximate more nearly to ideal blood

Secondly, mixing of several bloods has the effect of averaging out the agglutinin concentration and producing a final titre which is so low as to be harmless

The use of compressed air Jorda (1939) stores blood under a pressure of two atmospheres He claims that this gives him a method of automatic bacteriological control of the blood (p 399) and a positive pressure for introducing the blood into a vein For the details of this method his own paper should be consulted (Jorda, 1939)

The addition of sodium citrate

As it is undesirable to expose the mouth of the bottle to the air for longer than is necessary, the citrate should be added to the bottle before it is autoclaved So far as is known at present the quantity will be the same as when the blood is intended for immediate use, that is to say 10 c c of 3 per cent sodium citrate to every 100 c c of blood drawn Dry sodium citrate has been used for this purpose and so also has 30 per cent, in which case the quantity will be 1 c c of 30 per cent per 100 c c of blood As reported in a later section, when larger amounts than 0 3 gramme to 100 c c of blood is used, the onset of haemolysis is accelerated It is possibly an advantage to dissolve the citrate in a minimal quantity of water, so that the volume of fluid introduced into the blood may be as small as possible Other anticoagulant solutions are discussed on p 187

The technique of collection of blood for storage

If the McCarthey bottle is used the technique of collecting for storage purposes is exactly the same as that described for the withdrawal of blood by the closed method on p 8 The tubing carrying the donor needle is washed through with sodium citrate before making the venipuncture It will be unnecessary to make any negative pressure as a rule especially if the tubing to the donor is kept really short

Blood should also be collected into separate tubes for *cross matching* and for the *Wassermann reaction* if the donor is unknown I find that this is most easily done after the collecting flask has been filled the in flow tubing is temporarily pinched while the bottle is being disconnected A few c c are now allowed to run into a test tube (no citrate) for the Wassermann reaction and a few drops into another tube containing some 3 per cent citrate for cross matching The latter tube should be strapped to the side of the bottle

In some hospitals there is no provision made for cross matching without opening the main bottle This is unsatisfactory because supposing the cross test shows incompatibility the bottle will have been opened unnecessarily and needless waste of blood will occur Once the container has been opened it must be regarded as being potentially contaminated The technique recommended above avoids the danger of contamination as the main reservoir is left undisturbed

Accurate and prompt *labelling* is important The blood group and date of collection must be clearly marked and the blood stored separately until the Wassermann reaction is known The blood should *not* be left standing *exposed to light* and if it is to be taken some distance it should be covered with a cloth As freezing must be avoided it is not safe to keep the blood in the usual domestic refrigerator

CONDITIONS OF STORAGE

Duration of storage

The conditions must be such that the blood retains its beneficial qualities without acquiring any harmful ones Human blood transfusion is said to have been successful after as long as

four weeks' storage, but my own opinion is that *this is far in excess of the safe period.*

Recent contributions to the medical press in Britain have tended to give a false sense of security in regard to the safe period of storage. A point is made in some of these reports that no rigors have followed the transfusion of fourteen-day-old stored blood, but if a careful examination of the case histories is made it will frequently be found that the patients were gravely ill at the time, or subjects of advanced carcinoma. Such individuals have not the necessary powers of resistance to produce a reaction, and cannot be taken as reliable controls in determining the safety of stored blood.

The danger of stored blood resolves itself into the question of haemolysis, since infection is more easily prevented, and though chemical changes in the plasma have hardly been investigated, they are probably of minor importance. It is occasionally stated that slightly haemolysed blood is no contra-indication to transfusion, but even if this is true, the biological activity of degenerate cells can hardly be very great.

Onset of haemolysis.

Haemolysis in stored blood is due to the increasing fragility of the red cells with the passage of time. The onset may be identified by determining the fragility of the cells in hypotonic salt solution, and by observing the actual haemolysis with the naked eye or spectroscope. The morphology of the red cells can also be observed by direct microscopic examination of the cellular elements in fresh and stained films.

The time of onset of haemolysis varies with the conditions of storage. The most influential factors are:

(i) The nature of the anticoagulant solution.
(ii) The temperature.
(iii) The strength of citrate.
(iv) Trauma.

(1) The nature of the anticoagulant solution:

(*a*) Sodium citrate: 3 per cent., see p. 305.

(*b*) I.H.T. solution, used by the Moscow Blood Transfusion Institute.

(*c*) Isotonic glucose-citrate solution.

The addition of glucose to the sodium citrate appears definitely to delay the onset of haemolysis (Rous and Turner 1916) Bagdassarov (1937) of Moscow found the fragility of the red cells was increased steadily and equally up to the eighth to tenth day whether the preserving fluid was sodium citrate only or a glucose–citrate solution After the eighth day however, the fragility of the cells stored in citrate only rapidly increased but the resistance of the cells stored in glucose–citrate remained stationary until the thirtieth to thirty fifth day After this the discoloration of the plasma gradually extended

Possible objections to the use of glucose are that it tends to caramel on autoclaving and that it provides an excellent culture medium for organisms The glucose also breaks down in time with a resultant rise in lactic acid content of the stored blood

(ii) **The temperature** As far as is known at present the refrigerator should be kept at a constant temperature of 4°–6° C Temperatures below zero will result in the blood becoming frozen —a physical change associated with haemolysis and marked toxic effects if it is transfused after thawing A typical haemolytic reaction following the use of frozen blood is reported by Alverov (1935) The blood which was three days old showed evidence of haemolysis on warming but this was ignored Haemoglobinuria and jaundice followed the transfusion

(iii) **The strength of citrate** The effects of varying the strength of sodium citrate in the blood collected have been compared using 0 3 0 4 0 5 and 0 6 grammes to the 100 c c of blood

Visible haemolysis appeared first in the samples of blood containing the highest percentage of citrate that is to say 0 6 of a gramme per cent. (Thrower 1938)

Examination by the spectroscope showed absorption bands twenty four hours before haemolysis was visible to the naked eye

(iv) **Trauma** If there is any trauma prior to use during collection storage or transport the onset of haemolysis is always accelerated

MORPHOLOGY

Bagdassarov (1937) in a study of the morphology of the formed elements in blood (stored at 6° C and containing 10 c c

of 3 per cent sodium citrate in 100 c c of blood), found that the red cells remained normal in size until the tenth day, after which small and crenated forms appeared, by the twentieth day many of the cells were disrupted and pale microcytic forms were present The neutrophil leucocytes showed degeneration earlier than the erythrocytes and were not discernible by the fourteenth day, the lymphocytes and platelets appeared to be most resistant

SUGGESTED RULES FOR STORING BLOOD

Period of storage.

My own observations with blood taken from living donors citrated with 10 c c of 3 per cent sodium citrate to 100 c c of blood and kept away from the light at 4° C suggest that under these conditions it is not safe *to use blood after it is more than eight days old* My personal preference is to avoid blood more than seventy-two hours old

Naked-eye inspection.

If possible, examine the flask in the refrigerator before moving it, or if a better light is necessary remove it very gently Careless handling at this stage by mixing the plasma and cells will make it impossible to decide whether haemolysis is present or not It will be remembered that citrated blood settles in layers on standing

(i) A superficial layer—the citrated plasma
(ii) An intermediate layer—leucocytes and platelets
(iii) The lowest layer—red corpuscles

If there is no haemolysis present the upper limit of the red cells shows a clear cut line Haemolysis first appears at this level and blurs the line as the pink coloration permeates through the intermediate layer into the lowest part of the supernatant plasma

Contamination.

It has been the observation of those who have had most experience in the use of stored blood that if infection should occur, it will show macroscopically either in the form of small specks on the surface of the separated plasma or as haemolysis In the early days infection was the bogy which retarded the

wider practice of the method In Moscow both Judine (at the Sklifassovsky) and Bagdassarov (at the Institute) the former using cadaver blood and the latter blood from living donors used to make cultures before transfusing the blood but this method of control has since been given up because they found that if infection was detected bacteriologically it was also visible to the naked eye In practice the proportion of infected bottles is extremely low If a bottle or flask is opened to test its sterility during the course of conservation organisms may find their way in during the manipulation so that this practice should be condemned If on the other hand examination is delayed until the bottle is to be opened for use no result can be obtained in time to be of any value For these reasons an impeccable aseptic technique for collecting must be established and the macroscopic appearance of the blood carefully noted before injection

Automatic bacteriological control

Jorda says that automatic bacteriological control is possible if the haemoglobin of stored blood is converted to oxyhaemoglobin In his tube' the blood is stored under a pressure of two atmospheres exerted by filtered air He says

'Physiologists have shown that a pressure of 10 mm Hg is enough to convert 99 per cent of the haemoglobin to oxyhaemoglobin if the blood is in contact with oxygen This action takes place in our tube owing to the amount of oxygen in the air All the blood pigment is changed to oxyhaemoglobin and the blood becomes a ruby red

If the blood is accidentally contaminated the organisms will not grow unless they are aerobic because the growth of anaerobic organisms is inhibited by the oxygen in the tube and by the intense oxygenation of the blood The growth of aerobic organisms will take place at the expense of the oxygen in the tube and since the tube is sealed the oxyhaemoglobin will be reduced and the blood change from ruby red to dark red thus showing that the blood is not sterile If the bacterial action proceeds further the blood pigment alters to haematoporphyrin and the blood turns black This fact is fundamental to our technique and allows us to control the sterility colorimetrically

Do not shake

The fragility of the red cells increases daily with storage and the effect of shaking is proportionately accentuated For this reason the supernatant plasma and the red cells should be mixed by gentle rotatory movements

Opportunities for damaging the red cells arise *during the collection of the blood if the blood is allowed to flow on to the sides of the flask* or if it is too strongly shaken *during preservation*, if the bottle is repeatedly lifted out of the refrigerator for examination, *during transport* if it is agitated, and *prior to use*, if the supernatant serum is mixed with the cells too vigorously

A severe haemolytic reaction following the injection of blood —Group O conserved fifteen days—which had been shaken prior to injection is reported by Alverov (1935) A similar quantity of the same blood collected at the same time, but which was not shaken, was given to another patient after the same interval of conservation without any reaction

Clots.

Small clots do occasionally form in spite of adequate citration If the clots are microscopic they will probably do no harm, and if they are larger they will not pass through the needle To be on the safe side, however, it will be best to filter, if only to ensure no mechanical blockage in the course of the transfusion

If the blood is being transferred to another container, filtration through a funnel lined with sterile gauze will be an easy matter If the blood is being injected directly from the bottle in which it has been stored, some form of intervening filter should be inserted in the circuit between flask and patient Any of the types mentioned under blood filters, p 243, will serve the purpose

Warm gradually.

Rapid transfusions Fifteen minutes at least should be taken to bring the blood up to the required temperature for injection, or rigors will follow regularly Ideally the blood should be transferred from the ice chest to a laboratory incubator half an hour before it is required for use Overheating causes haemolysis, and this will occur more readily with conserved blood because of the increased fragility of the red cells If there is no time to warm the blood slowly it is far safer to *inject the first 100 c c at a temperature below the* optimum

Transfusions at a drip rate. *It* must be remembered, however, that the injection of *ice cold* blood is dangerous I

have known a drip transfusion started with blood received directly from the ice chest and a sharp rigor follow immediately. One must make sure then that the blood in the reservoir is *not below room temperature* even if it is being introduced at a drip rate when accurate temperature control is not quite so important

Administer slowly

Transfusions of stored blood should be given at a drip rate unless the circumstances are exceptional

The rule to introduce the blood slowly applies to most transfusions but should be rigidly applied here as undetectable haemolytic changes may have taken place and these will usually cause a disturbance early in the transfusion. If one is on the look out for the symptoms the transfusion can be stopped before too much blood has been injected

Statistics of Reactions following Blood Transfusion in Man using Stored Blood taken from Living Donors

Reported by	Period of conservation	Number of transfusions	Reaction per cent: Total per cent	Medium and severe	Mild
Alverov (U.S.S.R.)	1–5 days	53	69.9	64.1	5.8
	6–10	93	69.4	60.9	8.5
	11–15	19	83.1	66.6	16
Mayo Clinic (U.S.A.)	1–12	140	12.8		
Bagdassarov (Moscow)	1–14	*790	6.0		
Elliott *et al.*	4–10	50	16	8	8
Biddle & Langley	1–14	150	15	5	10

The above table includes all grades of reaction from the mildest to the most severe

A mild reaction is taken as one in which there is slight discomfort following the transfusion with a rise of temperature up to 100° F

A medium reaction as one associated with a chill or rigor

A severe reaction as one associated with haemolysis as shown by jaundice haemoglobinuria or anuria

CADAVERIC BLOOD

In investigating the subject of cadaveric blood transfusion, evidence must be drawn in the main from the work accomplished in the U S S R in the last ten years In Russia the method is firmly established, and it is from Professor Shamov (1937) of Kharkov, Professor Judme (1936) and Dr. Skundina (1935) of Moscow that the data of its practice can be obtained.

In 1927 the first experimental work was undertaken by Shamov. He used blood obtained from dogs after death for injecting into living dogs, and established the safety of the procedure experimentally. His success with dogs led him to realize the possibility of using human cadaveric blood for transfusion, but he had no opportunity of carrying the idea into practice at his own hospital However, he communicated his observations to Professor Judino, who, with the greater facilities at the Central Emergency Hospital in Moscow, was able to demonstrate the efficacy of human cadaveric blood transfusion as foreshadowed by Shamov.

The first transfusion with cadaveric blood at the Central Emergency Hospital was performed on 23 March 1930 Circumstances invited the experiment A young suicide, already in extremis from loss of blood, and the corpse of an elderly man, recently dead from a fractured skull, lay in the same receiving room Both patient and corpse happened to be of the same blood group, and Professor Judine, unquestionably free of all moral responsibility, performed successfully the first human cadaveric blood transfusion. A little later chance contrived another set of circumstances which carried Professor Judine a stage farther. Some citrated cadaveric blood left over from a transfusion was placed in the refrigerator three days later a patient with intestinal haemorrhage required an immediate transfusion No donor was available, and the stored blood was successfully used. Thus the use of stored as well as fresh human cadaveric blood became a practicable possibility. It only remains to note the remarkable observation of Dr. Skundina (1935) of 'spontaneous fibrinolysis' which crowned the investigations in Moscow. Since then progress has been confined to elaborations of technique.

Professor Shamov (1937), from his experiments with dogs, considered that it was necessary to establish

(i) That cadaveric blood is not infected at the time of its withdrawal

(ii) That cadaveric blood is not toxic

(iii) That cadaveric blood has its vital qualities unimpaired

(i) This was done by bacteriological examinations of the blood and tissues taken under various conditions They showed that infection of tissue in a dead body depends upon two factors The first is the nearness of the tissue or organ to the chief focus of infection—in healthy animals this is the gastro intestinal tract—whence it spreads rapidly by the portal system to the abdominal organs At room temperature the blood in the mesenteric veins becomes infected about twenty hours after death and the liver is the earliest abdominal organ to be infected The second factor is the temperature at which the cadaver is kept In the most favourable conditions for preservation—about freezing point—the tissues nearest to the focus of infection do not begin to be infected until after ten days and the more distant organs such as the brain may be preserved for twelve days or more The practical deductions from these results were

1 The portal blood should not be used for transfusion purposes

2 The cadaver should be kept in a cool place after death

(ii) To determine the toxicity of the cadaveric blood of dogs the animals were killed by strangulation and the blood withdrawn and citrated This had to be done within ten hours of death as after this time the blood clotted and could not be collected The blood volume red cells and haemoglobin were previously estimated When the blood had been thus obtained a live dog was brought into the operating theatre whose blood volume haemoglobin and red cells had been determined Paraffined cannulae were tied into its carotid and internal jugular veins Through the carotid blood was drained from the animal through the internal jugular was injected the blood taken from the dead body As much as 60 per cent of the total blood volume was *withdrawn and cadaveric blood substituted without toxic* symptoms being produced

(iii) The next question to decide was whether the red cells could live and function after their transplantation into a living

animal The answer to this would appear to have been given by the observations made in the previous paragraph It might be objected, however, that the transfusion acted purely mechanically by restoring the blood volume To settle this question, a series of experiments was arranged involving a much greater blood loss Animals were bled to 70 per cent of their total blood-volume, after which blood ceased to flow from the carotid By injecting large quantities of saline to wash out the blood vessels, the degree of blood exhaustion was raised to 90 per cent This figure is incompatible with life for more than a few minutes, and only the transfusion of living functioning blood can keep the animal alive, as shown by control experiments A transfusion of cadaveric blood withdrawn ten hours after death was then given, and in each case the animal revived, and progressed to normal convalescence In later experiments it was found that the phagocytic activity of the leucocytes was also unimpaired in the cadaver up to ten hours after death

EXPERIMENTAL WORK IN MAN

Shamov's work was supplemented by the subsequent work of Barenboim and Skundina (1932), who studied the gaseous exchange in dog and man before and after the transfusion of cadaveric blood Their investigations showed clearly that the great decrease in the oxygen exchange after a haemorrhage was followed by a sharp increase if a cadaveric blood transfusion was given This established the fact that the oxygen carrying power of the red cells is undisturbed in freshly drawn human cadaveric blood, and showed that the red cells and leucocytes of a dead body ten hours after death still retain their full vitality and are able to function physiologically quite as well as the cells of normal blood

Since the onset of infection in the portal system is earlier than in the extra abdominal veins, it was thought that it would be an extra safeguard if the portal blood were excluded when the body was drained, even though it was said not to become infected for twenty hours after death This, however, offered considerable technical obstacles Fortunately, about this time, A V Rusakov (1934), pathologist to the Sklifassovsky Hospital, was able to show that in spite of Indian ink and methyl blue

injections into the mesenteric veins of cadavers, blood collected forthwith from the jugular vein contained no trace of ink or dye In other words, blood collected from the internal jugular vein comes only from the upper and lower vena caval systems, that is to say, from the regions least subject to infection

In the first 200 transfusions of cadaveric blood, citrate was added as an anticoagulant, but after the observation made by Dr Skundina (1935) it was no longer required She noticed that the blood drawn for the Wassermann reaction (that is to say, without the addition of citrate) from cases that had died a sudden death, quickly coagulated in the test tube to form an ordinary clot and then reliquefied of its own accord in ¼–1½ hours It was immediately realized that from certain cadavers a supply of blood could be obtained which did not require the addition of an anticoagulant Fresh and stored uncitrated cadaveric blood was used with excellent results, and since then over two thousand transfusions of this kind have been given in Moscow

Fibrinolysis, that is to say, liquefaction of the coagulum, is by no means understood It is accompanied by gradual disappearance of the fibrin, but is apparently not due to digestive breakdown as the serum nitrogen is not increased It occurs in blood withdrawn from people who have died suddenly and from badly shocked patients, but not from people who have died after a long illness In severe peritoneal haemorrhage, a disaster accompanied by shock it is not uncommon to find the blood liquid, and this also may be due to liquefaction of the clot Certainly a severe shock is akin to death, and it may be that fibrinolysis is not connected with the actual death of the patient McFarlane reported fibrinolysis as a transitory property of the blood of patients immediately after operation From the practical point of view, liquefaction of the coagulum is an added guarantee that the patient did not die following a prolonged illness, and, what is more significant, such blood will not require an anticoagulant and may be regarded as whole blood

Technique of collection

The technique was shown to me by Dr Skundina The cadavers are kept in a cool room, and the blood is withdrawn within eight hours of death in winter and six hours in summer

The neck is prepared as for a surgical operation, and sterile towels are applied after the preparation of the skin Instruments, ligatures, and cannulas are taken from a sterile drum A two inch incision is made along the middle of the posterior border of the sternomastoid, the internal jugular vein is exposed and two ligatures are passed behind it and drawn to the extremities of the wound The vein is opened by scissors in two places, first above and then below A large gaff shaped cannula is inserted into the upper end and a straighter cannula below which reaches into the right auricle, and both are tied in The high Trendelenburg position is now adopted and about 1½–2 litres of blood are drained from each cannula by way of rubber tubing into wide open mouthed bottles standing on the floor A separate bottle of blood is collected for the Wassermann reaction, grouping, and blood examination No citrate or other anticoagulant is added to the blood The bottle necks are closed with sterile gauze caps each bottle is labelled with the date and necropsy number and placed in the refrigerator at 3° C It is kept or discarded according to the result of the necropsy made by the pathologist and is relabelled as soon as the haematological report is received

The quantity of blood collected varies, depending on a number of conditions, the most important being rigor mortis If an attempt to draw off the blood is made while rigor mortis is present only a small amount will usually be obtained It stands to reason also that the corpses of persons dying from injuries, after a considerable loss of blood either externally or into the cavities, will yield less than uninjured bodies The selected material yields an average per cadaver of 900–1,500 c c in deaths from trauma and 1 5–2 5 litres (often 3 5 litres and sometimes even over 4 litres) in uninjured cases

Storage of cadaver blood.

Cadaver blood is used up to and including the tenth day It is sometimes used after longer storage, but not from choice, as the fragility of the red cells increases markedly after the tenth day, and haemolysis results Judine says that a slight degree of haemolysis is not a contra indication to using the blood, and a transfusion of haemolysed tenth day blood has been given without any reaction In practice however, in a large hospital with

a constant demand for blood transfusion, the conserved blood is generally used within a few days, that is to say, before haemolysis has had time to occur

The conditions affecting the storage of cadaver blood are the same as those governing the use of stored blood from living donors, and were considered in that section

Special conditions governing the selection and use of cadaver blood

(i) *Suitable cadavers* The cadaver should be that of a person who died some form of violent or sudden death such deaths are usually unassociated with any general disease and provide the conditions necessary for spontaneous fibrinolysis Examples include angina pectoris, coronary thrombosis, cerebral haemorrhage and embolism, death by strangling hanging or electrocution, by gunshot and by street or other accident

(ii) *Unsuitable cadavers* Cadavers which should be rejected include those after

- (a) Death from sepsis, cancer, tuberculosis, or any of the chronic diseases
- (b) Death from drowning as the fluid in the lungs passes into the blood and causes haemolysis (Judine)
- (c) Cadavers with large open wounds
- (d) Death from poisoning

(Cases of fractured base of the skull and internal haemorrhage can be used)

(iii) The supply of cadavers must be considerable if they are to be the sole source of supply of blood for an institution In practice such conditions rarely exist, although the Central Emergency Hospital in Moscow may be quoted as an exception In Moscow all cases of sudden death in the streets and public buildings are taken to the Sklifassovsky,[1] and in addition to these a large number of accident cases also find their way to this hospital Thus a large supply of healthy cadaver material

[1] The Sklifassovsky Institute or Central Emergency Hospital so named after the well known Russian surgeon Known as the Sheremetief Hospital before the Great War It was then the Salpêtrière of Moscow, but it was renamed and reconstituted after the October revolution of 1917 like many other public buildings and institutions in the Soviet Republic

enables this particular institution to be independent of other sources of blood for transfusion purposes.

(iv) After death and until blood is withdrawn the cadaver should be kept in a cool place: warmth accelerates the onset of infection.

(v) The blood must be withdrawn before the onset of infection This does not occur under average conditions of storage of the cadaver in less than twenty hours To be on the safe side Judine advises withdrawal of the blood within six hours of death *in summer and eight hours in winter.*

Summary

The value of *uncitrated* cadaver blood from the therapeutic point of view is that there are fewer post transfusional reactions than with citrated cadaver blood, a drop of 15 per cent being recorded (from 20 to 5 per cent) Moreover, Shamov is convinced that the increase of haemoglobin and red cells is higher than that usually observed after transfusions of an identical quantity of blood from live donors, and he believes this to be due to its sharp stimulation of the haemopoietic system From the point of view of selecting material the examination of the dead body for the presence of disease can be very much more exhaustive than *with a living* donor and, in addition, the grouping and serological tests can be made at leisure, and perhaps therefore with greater accuracy

Possibly, however, it is in the large volume transfusion that the cadaver source of supply finds its greatest usefulness. Here its value is twofold—it supplies the quantity, and it is no easy matter to obtain a large number of donors at short notice, and, even more important, it supplies the quality, that is, a large amount of blood, all of the same group coming from the same donor, which must be a much safer arrangement than *mixing* the blood of a series of different donors. What *is more*, the Wassermann reaction will not need repeating as in the case of separate donors, and the usual complicated organization will be simplified many times. Finally, there will be great economic advantages.

On the other hand, there are many practical difficulties. In this country a coroner's order of necropsy is necessary and there

might be too much delay before getting access to a cadaver. There are no central mortuaries as in Moscow, so that collection and transport organization would be much more complicated, and a corpse is surrounded by an atmosphere of sentiment which would undoubtedly be antagonistic to the use of blood from this source. The question, however, can be conveniently shelved for the moment, since the supply of blood from voluntary living donors more than equals the demand in this country.

The important point is that we know the possibility of using cadaveric blood, and if circumstances require it we shall not be ignorant of the method of procedure.

PLACENTAL BLOOD

In Montreal and Leningrad a new source of fresh blood for storage purposes has recently been exploited—namely, the placenta

Before using placental blood for clinical purposes the Montreal workers (Goodall *et al* 1938) felt that they must establish the safety of the procedure and at the same time anticipate certain inevitable criticisms based on age old maxims To this end they challenged the statements

(*a*) That if the blood be left in the placenta placental detachment from the uterine wall is hastened

(*b*) That in taking blood from the placenta one is depriving the new born of its rightful due and that one should wait until the contractions of the uterus have squeezed some of the placental blood into the foetal circulation

Effect on the mother.

To decide the question of placental detachment they proceeded as follows at every birth the clamp on the cord was released in the dependent position and the placenta was emptied, so that the cord lay flaccid where before it was quite turgid They found that the separation of the placenta was not prolonged or less complete than when the blood was not allowed to drain away This observation has been confirmed by Page, Seager, and Ward (1939)

Effect on the infant

Every child at birth has a well marked polycythaemia in other words an excess of red corpuscles so that further additions from the placenta would seem to be unnecessary This is supported by the observations of Page Seager and Ward (1939) who carried out blood counts on twelve babies whose placentae had supplied blood and upon twelve controls The blood was examined on four occasions prior to discharge from hospital and they found that there was no appreciable difference in the blood counts of the two groups

The Anticoagulant

The anticoagulant solution varies in strength and composition with different workers Howkins and Brewer (1939) advise the

use of 0 3 gramme of sodium citrate in 10 c c of sterile water—freshly prepared This is the same dosage and strength—namely 10 c c of 3 per cent sodium citrate to 100 c c of blood—that is advised elsewhere (p 182) for ordinary transfusion work and is probably to be preferred to the more complicated solutions that have been suggested The anticoagulant is added to the collecting flask immediately prior to collecting the blood Other solutions used have been

(i) By Grodberg and Carey (1938)—15 c c of sodium citrate 2 5 per cent per flask

(ii) By Page Seager and Ward (1939)—1 gramme of sodium citrate in 80 c c of physiological saline per flask

(iii) By the Moscow Institute of Haematology (Bagdassarov 1937) and by Goodall *et al* (1938)

Sodium chloride	7 0 grammes
Sodium citrate	5 0
Potassium chloride	0 2
Magnesium sulphate	0 004
Redistilled water	1 000 c c

25 c c of this solution is added to 100 c c of distilled water and the placental blood collected into the resultant 125 c c

Hawkins and Brewer (1939) and Page Seager and Ward (1939) abandoned this mixture early in their experiments as they found that haemolysis occurred earlier than when using a more simple citrate solution

Container—for storage

A bottle of about 200 c c capacity and a glass funnel are used The bottle and funnel are wrapped separately in cloths and sterilized in the autoclave

Technique of collection

When the baby is born the cord is tied and clamped and then divided The last six inches of the cord are cleaned with a sterile swab soaked in spirit The operator now changes his gloves and puts on a clean pair By means of the clamp the severed end of the cord is passed through a small hole in a specially made sterile towel and directed so that it drains by way of a funnel into the receptacle containing the citrate solution The clamp is then

removed With the release of pressure the blood is forcibly ejected into the funnel since the blood pressure in the cord is considerable, and the process can be aided by milking the cord between the fingers Pressure on the fundus by the nurse or assistant, hastens the emptying of the placenta

The towel so placed is to prevent contamination of the contents of the receptacle by any fluid that might run down the cord from the genital tract

The average amount collected

The average yield per placenta is not very high and is in the neighbourhood of 50 c c (Howkins and Brewer (1939), 47 c c) Some rather more optimistic figures have been reported Goodall *et al* (1938) 125 c c, Page, Seager, and Ward (1930) 80 c c, Grodberg and Carey (1938), 105 c c

Grouping and cross-matching.

When the blood has been collected in the flask a few drops from the end of the cord are taken in test tubes, one into citrate for grouping, the other into an empty tube for the Wassermann, if the mother's blood has not already been tested for the reaction

Blood grouping is necessary Babies at full term have a fixed blood group because the agglutinogen factor in the corpuscles is fully developed (p 274) An infant's blood group is not necessarily the same as that of the mother, so that routine typing of placental blood is essential

Storage

The flask and tubes are labelled with the patient s name and the date and are transferred to a refrigerator at a temperature between 2° and 6° C

Sterility tests.

Reports as to the sterility of placental blood are somewhat conflicting Brewer and Howkins (1939), examining fifty samples, taken from consecutive placentae of normal births at term found that 22 per cent of primary cultures were contaminated The infecting organisms were for the most part saprophytes and comprised *Bacillus subtilis* group coliform bacilli, white staphylococci, and *Bacillus pyocyaneous* These

represent air borne skin or genital tract contamination Goodall *et al* (1938) (number of cases not quoted) Godberg and Carey (1938) (76 cases) report uniform sterility Page Seager and Ward (1939) found fourteen out of fifteen samples sterile and the single exception grew what was regarded as a non pathogenic organism It is interesting to note however that these workers state that upon changing the personnel of the collecting team three out of five subsequent specimens were contaminated It appears therefore that a strict technique must be closely adhered to and that in all cases the blood should be cultured

Contra indications

Only normal clean deliveries should be used All infected and potentially infected cases should be excluded Placental blood will of course not be taken in cases of obvious transmissible disease in either mother or child nor will it be taken where the membranes have ruptured more than forty eight hours before delivery or in cases of definite prematurity or multiple pregnancy If any accident of the third stage arises or if the child requires resuscitative measures the collection of blood will naturally be abandoned in favour of the more important procedure In cases of marked asphyxia the amount of blood in the placenta is in any case so small as to make it worthless

Reactions

There is insufficient data Probably the reaction rate is similar to blood taken from other sources that is to say increasing progressively with the period of storage

Length of storage

There is insufficient data

Alleged advantages

General (i) The placenta would appear to provide an inexhaustible source of blood which can be used immediately or after storage

(ii) In any large institutions the groups of the different samples of placental (foetal) blood will be proportionately the same as in the recipient The supply of each group therefore

will approximate the demand for each group A maternity section of a general hospital proportionate in size will be able to give enough blood for the needs of the whole institution

(iii) The economic advantages are comparable to those associated with the use of cadaver blood and lack many of the problematical features of the latter

Particular (a) Placental blood has a high cellular content the cellular strength is nearly 150 per cent of the adult and averages 7½ million red corpuscles per cubic millimetre

(b) Foetal blood contains from 20 to 30 per cent more haemostatic power than that of the adult This increase is gradually lost in the ten days following birth From the point of view of transfusion this phenomenon would appear to be an advantage in transfusing bleeding cases

(c) The absence of food allergens

Summary

Placental blood has not yet been on trial for a long enough time for any final or dogmatic statement to be made It would seem however that the initial optimism is not entirely to be fulfilled

The position as it appears to-day has been well summarized by Howkins and Brewer (1939) They point out that the average *yield* per case is small—certainly not more than 100 c c and usually less—so that five to ten samples would have to be mixed to produce the quantity of blood required for an ordinary small volume transfusion The manipulations necessary for mixing must also increase the opportunity for contamination Furthermore it is questionable whether this extensive pooling of several bloods although of the same group is entirely devoid of the risk of sub group agglutination reactions (see also pp 268 304)

The question of *sterility* also arises One cannot overlook the fact that Howkins and Brewer found 22 per cent of fifty samples contaminated with air borne or genital tract organisms It is true that in this series no individual operator was made responsible for the collection of the blood which was carried out by the ordinary trained staff of the labour ward If however the storage of placental blood is to be a practical proposition it should be possible to achieve this without a special collecting

team such as Page Seager and Ward (1938) found necessary if sterility was to be assured in a reasonably high percentage of samples Lastly even if sterility can be assured by a careful collecting technique the small yield obtained together with the extra burden thrown upon the labour ward and bacteriological staff makes it unlikely that placental blood will in peace time take the place of the well organized voluntary donor source which it is our good fortune to have established in this country

Although in my opinion it is undesirable that placental blood or indeed any form of stored blood should be preferred to fresh blood it is possible that the placenta may be a useful *adjunct* to the living donor source particularly for emergency purposes

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CHAPTER XXI

SELECTION OF DONORS FOR ENROLMENT IN A TRANSFUSION SERVICE

GENERAL CONSIDERATIONS

Sex.

Both males and females are acceptable In the London Service (1938) 20 per cent of the donors were women In 1937 there were also women donors in the Berlin, Budapest, Rotterdam, and Montreal Services, and in Leningrad (1937) 66 per cent of the professional donors were women In the New York, Paris, Copenhagen, and Vienna Services the donors were 100 per cent male

Age.

The age does not matter within wide limits Any one between the ages of 18 and 60 may be considered

Physique.

The stature and weight should approximate to the normal. Exceedingly large or very small people are better rejected

Status.

The married or single status has no significance in the selection of donors as there is no reason why married individuals should not be as healthy as the unmarried Marriage, however, involves other ties and is a frequent cause of a member withdrawing

MEDICAL EXAMINATION

CLINICAL, HAEMATOLOGICAL, BLOOD GROUPING

Clinical.

The prospective donor should be (a) in good physical health and (b) have good elbow veins

(a) **Physical examination.** A history of past illnesses such as old tuberculous lesions, malaria, or syphilis will exclude Protein sensitivity, in the form of asthma, hay fever, or urticaria, should be inquired for, and affected individuals are probably best

refused membership, although the tendency is for transmission of sensitivity to occur only during an active phase

A clinical examination must always be made to exclude the presence of any active disease, especially apical tuberculosis, valvular disease of the heart, or pleural effusion An abnormally elevated or lowered blood pressure will contra indicate acceptance An X ray of the chest may be advisable in certain cases

(b) **Elbow veins.** The elbow veins must be seen or felt without difficulty Donors with very small veins or veins which are invisible are best refused In those accepted the character of the veins should be noted—whether excellent, good or moderate —so that those with excellent veins can be reserved for emergency purposes and the moderate veins sent to the more experienced surgeons

Haematological.

The haemoglobin should not be below 95 per cent It is generally unnecessary to do a blood count

Blood grouping.

The blood group should be determined by putting up the donor's cells with stock sera A and B of high titre (not less than 1/100), and this finding confirmed by regrouping, putting up the donor's serum with stock cells A and B

MEDICAL SUPERVISION

In the interests of the donor's health it is advisable to lay down certain conditions and limitations associated with his service

1. Frequency of service.

In a *voluntary* service no chances can be taken of overtaxing the haemopoietic system, and service should be limited to four times a year for a man and three for a woman These time intervals apply to individuals who have donated the average volume at a time of 500–600 c c Individuals who have given only 200 c c , for example, can be allowed to serve again within the three month period Women can serve while *menstruating* with absolute safety Quite apart from questions of health,

more frequent service and its resultant leave of absence from business might antagonize employers

2 Amount withdrawn

The amount of blood withdrawn at one time should not exceed 600 c c This is approximately one tenth of the total blood volume Withdrawal of greater amounts than this are apt to be associated with faintness and automatic arrest of the blood flow A voluntary donor who faints is not likely to offer his services again

3 Cutting down

Cutting down to expose the vein by dissection must be absolutely forbidden whatever the circumstances Any infringement of this rule should be followed by the removal of the institution concerned from the list of hospitals supplied by the service Cutting down apart from the inconvenience and even risk to the donor straightway reduces his efficiency as a member of the service If cutting down is necessary either the donor s veins are unsuitable and he should not have been passed as a member of the service or the necessary technical skill is lacking in the operator concerned

4 Re examination

Donors should be re-examined from time to time in order to confirm that their health is not being adversely affected This meeting between Medical Officer and donor is of considerable importance in maintaining the unity of a voluntary service and gives an opportunity for reassuring the donor that all is well with his physical condition a fact often disputed by anxious relatives and friends who only too often persuade an active member to withdraw on the grounds that his health is being impaired

In a voluntary service it has been found that re-examination after every tenth donation is adequate On this occasion a physical examination should be made the blood pressure taken haemoglobin estimated and the Wassermann reaction repeated In voluntary services the incidence of syphilis after enrolment appears to be nil For this reason repetition of the Wassermann

reaction before each transfusion becomes unnecessary In the London Service no case of syphilis transmitted by blood transfusion has occurred since its formation in 1921 If the donor shows any tendency to anaemia—and this is unusual if the number of services per annum are limited—he should be told not to serve again for six months, and in the meantime iron in some form should be prescribed

5 Effects of withdrawal of blood upon the dooor.

Immediate. Faintness may occur if the blood is withdrawn in a sitting position, if it is withdrawn too rapidly if too much (more than 600 c c) is withdrawn or if the donor assumes the upright position too quickly after the transfusion

To avoid faintness, the donor should always lie in the supine position, excessive negative pressure should be avoided, not more than 600 c c should be withdrawn at a time and he should lie for ten minutes after the blood letting and then slowly sit up again

Delayed. From observations on donors immediately before and at intervals after transfusion, Brewer (1933) has found that for the average donation of 400–600 c c the haemoglobin drop is from 8 to 12 per cent This is not immediate, but takes place over the succeeding three or four days The time taken for the haemoglobin to return to its pre transfusion level is usually seven to fourteen days The physiology of the restoration of blood volume has been considered on p 135

6 Selection of donors for emergency transfusion

Relatives or friends of a patient who present themselves in an emergency must be as carefully examined as time permits Their selection should be carried out as indicated on pp 90, 256

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DETAILS OF DIFFERENT BLOOD TRANSFUSION ORGANIZATIONS

Service	*Voluntary or Professional*	*Number of Members*	*Age*	*Sex*	*Frequency of service per annum*	*No. of transfusions per annum*
Berlin	Professional	282	21–50	80% M 20% F	12 times	721 *1937*
Budapest	Professional	75	21–25	95% M 5% F	8 times	April–June 240 (1936)
Copenhagen	Voluntary	430	over 18	90% M 10% F	12 times	515 (1936)
Leningrad	Professional	1 004	18–40	66% F 34% M	8 times	4 000 (1936)
Paris	Professional	672	over 21	100% M	12 times	6 209 (1936)
Rotterdam	Voluntary	350	21–60	75% M 25% F	4 times 400 c.c. limit of donation	108 (1936)
Stockholm	Professional	300	18–40	99% M 1% F	12 times	768 (1936)
New York	Professional	1 800	21–40	100% M	12 times	9 280 *1937*
London	Voluntary	2 378	18–65	80% M 20% F	Off for 1 week per 100 c.cs. M 4 times F 3 times	6 628 *1938*
Montreal	Voluntary	121	21–50	M 92 F 8	4 times	190 *1937*

Interesting points in this table are

(I) The London service has the largest active list of donors of any service, followed by Leningrad.

(II) The Leningrad service has the largest number of women donors (more than 2 : 1) followed by London.

(III) The professional services allow their donors to serve on an average once every 3–6 weeks.
The voluntary services allow their donors to serve on an average once every 3–6 months.

CHAPTER XXII

THE VOLUNTARY OR 'BRITISH' SYSTEM OF RECRUITING DONORS COMPARED WITH THE PROFESSIONAL SYSTEM

Definition

A *voluntary* system is one in which the donor receives no payment other than expenses In the London Service these amount to less than one shilling for service

A *professional* system is that in which the donor receives payment for his donation, usually in direct ratio to the number of cubic centimetres of blood withdrawn

This country has, from the first, placed its faith in voluntary blood transfusion services abroad, on the other hand the system of employing paid donors is almost universal for example, in the United States and throughout Europe except in Holland and Denmark It is regrettable that there are still a few professional services in Great Britain and it is to be hoped that further organizations of this kind will be discouraged Of the numerous practical advantages of the voluntary system the most outstanding is the low cost factor

Cost

The average cost per case in which transfusion was given by members of the London Blood Transfusion Service in 1937 was 8s 6d (in 1938 it was only 7s 6d) in Liverpool the corresponding figure was 7s , in Birmingham 16s , in Manchester 13s 6d , and in Bristol 1s 8d When these sums are compared with those prevailing under the professional system that is, £5–£7 per transfusion, the difference is instructive For instance if a voluntary system were to charge fees at the professional rates, the cost of running a service providing for 5 000 transfusions a year would be in the region of £30 000 Moreover, if all the services operating in this country were taken into consideration the annual outlay would be in the neighbourhood of £100 000 This sum would have to be met either directly or indirectly by the State, as is the case under professional organizations

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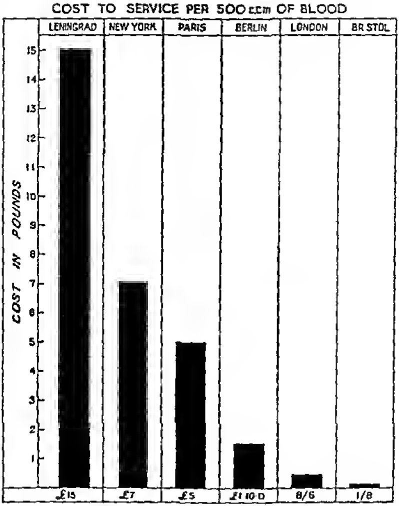

Fig. 64. The wide fluctuations in the rate of exchange must be borne in mind when assessing the significance of this diagram which militates most severely upon Leningrad. At the same time the wide difference in cost between voluntary and professional services is clearly conveyed.

The London Blood Transfusion Service has a steadily increasing surplus of income over expenditure which is independent of the results of any public appeals. For example in 1937 the income was £3 168 and the expenditure £2 300. This income relieves the patient of charges, the hospital of expenses and the

State of the necessity of subsidy It may be suggested that a State subsidy would popularize the system of blood transfusion and ease the minds of the doubtful by authoritative sanction This is questionable, since public opinion cannot at present be considered favourable to the advance of a service as specialized as that of blood transfusion For instance, its successes are treated (by certain sections of the press) only too often as miracles, and its failures as not unexpected catastrophes, whilst there are always relations and friends of donors to decry vicariously the pint of blood as Shylock s pound of flesh Also, State subsidy, in this country, of the less obvious of public services has usually been confined to those organizations so lacking in vitality that government interference alone prevents their collapse

Type of donor.

A further advantage of the voluntary system is that it supplies a better type of donor As a rule the member of the community who offers his services with no hope of remuneration is physically and morally preferable to the professional donor, whose altruism, it may be assumed, is prompted by no higher motive than his pocket The voluntary donor is not the type of person to contract disease or conceal it, and under the voluntary system the incidence of transmissible disease both in new members, and in those who are re examined after a number of transfusions, is nil In countries which follow the professional system, examination has been found necessary before each transfusion owing to the high incidence of venereal disease following enrolment This in addition greatly increases the work of the medical officer concerned

The type of donor is a consideration in another direction, in that the service affords manifest opportunities for *black-mail*. *In the voluntary system the incidence of extortion is reduced to* a minimum The type of individual who will give his blood voluntarily is the last person who is likely to turn a psychological somersault and become a blackmailer On the other hand, it appears that professional donors often demand extra remuneration for ill health which they claim has resulted from the transfusion Again, in a professional service it is in the interests

of the donor to obtain and answer as many calls as he can, even if it is necessary to resort to *forgery* or substitution to do so

The following statement was lately made by the Vienna correspondent of a London Sunday newspaper

> Wilhelm Huber held a certificate as a donor of blood for transfusions at a hospital here He received £3 for each transfusion He fell ill Doctors refused to renew the licence So he changed the entries in his certificate Discovered he has been given eight days in prison '

The other evil that of *substitution* is more dangerous If illness makes answering a call impossible, it has happened that a friend or relative of the donor has been sent in his place, for besides the opportunity of collecting the fee it is good to keep the business in the family As the result of this deception, passports with photographs of the donors have been instituted in most of the professional services The voluntary donor, on the other hand has no object in concealing illness or in substitution, and no case of this kind can be quoted Moreover, since the donor under the voluntary system serves only three or four times a year, it is not to be supposed that if passports were instituted in this country, he would have in his pocket, at the time he received a call, the official registration book given him some months previously

V *Health of the donor*

A factor of perhaps more importance in the organization of a voluntary system than of a professional is that in the case of the former the health of the donor is adequately safeguarded By limiting the *frequency of service* to four times a year and by forbidding *cutting down* upon the veins the health and efficiency of the donor in this country is not impaired

On the other hand in many countries where the professional donor is the rule service every six weeks and even more frequently, as well as cutting down are permitted

Therapeutically as in almost every other direction, the remunerative system is liable to become inferior to the voluntary in that if blood is to be paid for by the 100 c c the tendency may sometimes be to take too little Furthermore, large-volume drip transfusions must be almost impossible except for the very rich

Another advantage of the voluntary system lies in the opportunities it affords of *obtaining recruits* The professional donor may be tempted to corner the market he will in any case not be enthusiastic to create over production in perhaps his only stock in trade The voluntary donor on the other hand will not conceal the existence of the service from his friends and frequently proselytizes with the zeal of a new disciple

The above comparison of the voluntary system and the professional system may seem to the adherent of the latter to be unduly weighted in favour of the British system and too condemnatory of that working on the Continent and in the United States of America The only slight redress in the balance is the contention that the donor under the professional system must be available at times previously arranged and cannot refuse to answer a call The conclusion drawn from this is that there is not the delay in getting in touch with the professional donor that there is in calling up a voluntary donor But it must be remembered that under a well run voluntary service there need be no delays other than the inevitable ones produced by illness accidents or traffic congestion which may occur equally under either system

In travelling it is gratifying to compare the ease with which British Centres carry out their work as opposed to the multiplication of regulations necessary to ensure a professional service against abuse The impression received in visiting countries abroad is that the English system is regarded as hopelessly utopian and as characteristic a national phenomenon as the British Constitution

The cost of 8*s* 6*d* per case which includes the salary and other expenses of the medical officer the donor s expenses staff salaries and a twenty four hour service cannot be regarded as excessive In this connexion it is interesting to note that less than 50 per cent of the donors claim any expenses at all

In all services the main source of income may be expected to be derived from fees from private cases with a smaller benefit from public institutions It is suggested that when forming a new service reasonable charges to begin with would be five guineas for a private case one guinea to a State or municipal hospital and 5*s* to a voluntary hospital Other sources of

income are more precarious and will vary with the district served by the particular service and the methods of the responsible body On the whole flag-days matinees and the like are best avoided as the type of donor who makes up the bulk of the roll dislikes publicity of that kind

It may be argued that the financial problem is more acute in small towns than in large cities where opportunities of obtaining donations from private patients are considerably greater Experience does not bear this out and those contemplating forming a new service should not be discouraged on this account but should bear in mind that the area covered will not be so great and the administration costs will be less For this reason the figure of 8s 6d can be safely given as a maximum of expenditure per transfusion though it should be possible when only small areas are to be supplied with donors to run a service even more cheaply than this

CHAPTER XXIII

THE ORGANIZATION OF A VOLUNTARY TRANSFUSION SERVICE

THE PRINCIPLES INVOLVED IN THE FORMATION AND MANAGEMENT OF A VOLUNTARY SYSTEM WITH SPECIAL REFERENCE TO THE LONDON BLOOD TRANSFUSION SERVICE

IT was in 1921 that the first blood transfusion service in the world voluntary or professional came into existence in London under the auspices of the British Red Cross Society From the history of this service the principles governing the foundation and administration of a successful voluntary system can be deduced since the practice of more than fifteen years has overcome difficulties and culminated in the eminently practical and efficient system now in existence

The association of the British Red Cross Society with blood transfusion dates back to a day in 1921 when a request was received by the Camberwell division of the County of London Branch for a blood donor for an emergency case Four members of the division immediately volunteered their services and P L Oliver the Honorary Secretary of the division seeing that this was work most suitable for the Society seized the opportunity to prepare a list of members who were ready to volunteer for future cases

As time went on it became clear that the Camberwell division could not meet all the demands for donors that began to arrive and resort was had to the press Among those who responded was a rover scout who interested his organization in the work and the London Rovers adopted blood transfusion as one of their forms of service

At the end of 1925 the range of the work had increased to such an extent that problems of organization and technique and other difficulties had begun to arise These necessitated a somewhat more responsible governing body than had hitherto existed so the Service applied to the British Red Cross Headquarters to take over officially the conduct of the work This was done and a Committee representing hospitals the medical

THE LONDON BLOOD TRANSFUSION SERVICE 1921—1938

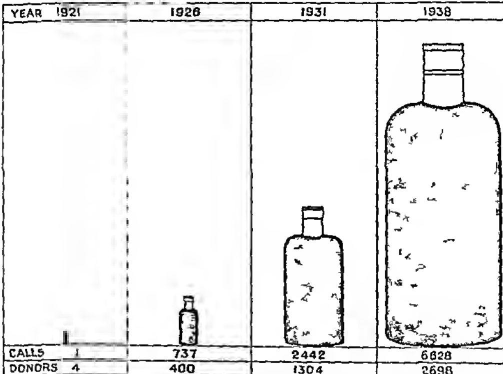

FIG. 65. This diagram shows the enormous increase in recent years in the use of Blood transfusion since the Great War. The figures represent the number of calls answered by the members of the London Service only. These amount to approximately one third of the total number of transfusions given per annum in the London area, the remaining donations being supplied by friends and relatives of the patient.

profession, the donors, and the Society itself was constituted. From this time the working of a voluntary service in London was assured, and nothing can show the success of the movement, both before and after its establishment as an organized system, more than the rapidly increasing number of calls for blood donors. In the earliest year, 1921, there was one call; in 1924 there were sixty-two; in 1927, 1,293; and in 1938 there were 6,628 (Fig. 65).

A study of the London Blood Transfusion Service to-day reveals the main principles governing the formation and management of a voluntary system to be those relating to the obtaining and retaining of donors. I am indebted to P. L. Oliver the honorary secretary of the Service for the substance of the account which follows.

OBTAINING THE DONOR

Lectures.

To obtain donors is easier then to retain them, and although the existence of donors is the *sine qua non* of the system, it is the retention of the goodwill and potential usefulness of the donor that gives to the service its coherence and success. To obtain donors who will become *permanent* members of the society requires judicious selection. Recruits in the London area come from two main sources. The bulk join as the result of lectures given to such organizations as Rover Scouts, Toc H, the Y.M.C.A., St. John Ambulance, and religious, literary, and social organizations of every kind. Although in emergency cases the services of constables and even firemen have been commissioned, members of callings such as theirs must, by the very nature of their work, be often unavailable, and in enrolling permanent donors people whose availability is so uncertain should be avoided. Nurses, medical students, and hospital porters should also be regarded as unsuitable, particularly in time of war, when they will have more important duties to perform. *No appeals for donors* are made at these talks, but a cinematographic representation of an actual transfusion is shown and pamphlets containing information and details distributed. Listeners are asked to consider in all its bearing the project of joining before they apply for a form of

enrolment, and no encouragement is given to enrol in the enthusiasm of the moment. In fact, potential recruits are compelled by various factors, such as examination for grouping and entry forms containing questions on accessibility and times available, to take some time to consider whether or not to join. The importance of this delay can be gathered from one or two examples taken from the disappointing results of broadcast appeals. A year ago a broadcast in the north of England invited recruits. There was a mass response, about 1,000 immediately asking for further information; of these 500 only became enrolled, and of these again less than 10 eventually became reliable donors. Another broadcast by a London hospital was equally ineffective in obtaining any permanent members. As the result of such experiences advertisement of this kind has been abandoned, although it may be suggested that a broadcast by an established blood transfusion service, asking not for recruits for itself but for general support for the system, might in the future be a means of giving confidence and help to those contemplating forming a local service.

The *personality* of the popular lecturer or commentator on blood transfusion is of immense importance in the psychological sphere for recruiting. Besides possessing the more obvious necessary attributes he should not, for example, stress unduly the guarantee of excessive protection of the donor, for this provident care against evil will frighten some and disappoint others; he should also contrive to present the service not as an act of heroism but rather as a privilege and hope, by so doing, to obtain the more permanent type of donor. In addition, it should be pointed out that membership involves no financial outlay and no inconvenience other than occasional loss of time.

Experience has shown that more volunteers are attracted by a *lay talk* from an obviously disinterested person, particularly if he is a donor himself, than by a medical man or hospital official who might be assumed to minimize any drawbacks or risks involved.

Recommendation

Besides those donors who join as the result of lectures, the other large section of recruits offers its services on the recom

mendation *of friends or relatives* who have served without untoward results Lately, some parents of donors have joined more or less from curiosity and have found the experience beneficial to their health A few as an expression of gratitude, join as a result of a transfusion given to a friend or relative, whilst a very few are ex recipients of blood who have recovered and offer themselves in turn

Other less effective methods of obtaining recruits are employed at various *times Of these the chief are the circulation of pamphlets* and publication in the *daily press* The success of these media depends largely on the nature of the given notice, though one or two general comments may be made Pamphlets produce results from those who are already interested but there is not much inclination to read them amongst the majority of people, to whom transfusion is somewhat remote and who are bombarded on all sides by printed matter The daily press might be of powerful assistance but up to the present the tendency has been to portray blood transfusion as an act of heroism if not of personal danger (see p 348)

The means of recruiting outlined above together with the fact that the system is voluntary give the London Blood Transfusion Service a reliable type of donor The increasing number of applications for membership in recent years has given the service a wide field for selection and since the demand for transfusions seems now to be nearing its maximum and the number of donors is still on the upward trend it should be possible to raise the standard of donors in London still more as regards accessibility of the veins, availability for service, and general enthusiasm

The organization of a Service is pre eminently one for a social service body whose members will make a point of keeping personal touch with the donors listening to their complaints even if unfounded noting holiday times temporary disabilities and *changes of address and conveying the occasional messages of* appreciation that are received No hospital official could spare the time from his multifarious duties to keep this personal touch to the front

RETAINING THE DONOR

The second great principle that emerges from a study of the London Blood Transfusion Service is that involving the retention of the donors in the system. To accomplish this it is of primary importance to take care of the donor's general interests and health by such methods as (1) an organization to deal with his grievances and criticisms, (2) the limitation of donations, and (3) by not cutting down on the veins. Also, consideration must be shown to the donor before, during, and after a transfusion, and this calls for interest as well as efficiency on the part of the hospital.

General interests

Under the system in force in London the general interests of the donor are entrusted to a special *committee representative of the donors* to which complaints and comments are forwarded for remedy and consideration. For matters of technique and practice in general, medical consultants particularly experienced in transfusion are co-opted. The main importance of such a body lies in the support which it gives the Executive of a service when the latter finds it necessary to remonstrate with a Hospital Board in the interests either of a donor or the service. These interests involve the investigation of complaints of delay, discourtesy, and technical faults, and of more general complaints such as excessive calling up of the universal donor.

General health

The general health of the donor is safeguarded by a *medical officer* appointed for that purpose. On the appointment of the first medical officer the effects of the new found confidence on the part of the donor was immediately shown in a reduction of the number of resignations and an increase in the pace of recruiting, and since 1931 the general influence of the supervision of the medical officer has been that of retaining old donors and attracting new.

The health of the donor in this country is also protected by *limiting the frequency* of transfusion to four times a year for a man and three for a woman. The result of this limitation is that

there is no danger that the haemopoietic system will be weakened by that alarming frequency of donations often encountered in professional services where service is, on an average, once a month, although it must be admitted little harm seems to come of it.

In America, a strong man by the name of Spike Howard claims to have served 800 times, and is still able to break iron chains across his chest, and in France, an undertaker of slight physique has served 900 times without effect on his good health.

What is perhaps more important is that this rule on the number of donations prevents the overtaxing of the goodwill of the members—an important consideration in the organization of any voluntary system

The health of the donor is also safeguarded by the rule *forbidding cutting down* on the veins Until 1926 cutting down was practised in 60 per cent of cases in London, with the result that by that year the majority of the original members of the service had to resign since they were unfitted for further donations of blood The usual plea for the practice was that a donor's veins were so inaccessible that the surgeon was obliged to cut down. However, in 1926, the dictum was laid down that if a vein were so inaccessible as to necessitate cutting down, the donor should never have been passed as suitable at the time of enrolment.

Personal treatment.

To retain the donor it is necessary not only to consider his general interests and health, but his *personal treatment* when actually serving at a transfusion The treatment of a donor in this direction lies with the internal administration of the hospital or institution to which he is sent, and not with the service. One may here recommend certain methods of procedure calculated to convince the donor that his services are appreciated and to inspire him with the willingness for a similar call in the future.

When a donor has been requisitioned a nurse should be instructed to go to the main entrance on his arrival and conduct him to the operating room or laboratory for cross testing. If any delay is likely, this should be explained and the reason given.

Sometimes donors have hurried away from business only to face a long wait at the hospital The inquiries which are made often reveal delay to have been totally unnecessary, although, of course, there are occasions when it is quite unavoidable To prevent waste of time by all concerned donors, on reaching the hospital should first mention that they have come to give a blood transfusion and then if asked, give the name of the ward and surgeon It has happened on a number of occasions that a donor has simply asked for a particular surgeon In such a case he has been told by a hospital official to whom he has not specifically stated that he has come to give a transfusion that the surgeon he wants is engaged—whereas that surgeon is actually in the operating theatre awaiting the arrival of the donor

When the donor has been received on his arrival at the hospital, he should be asked whether he would like some refreshment after the transfusion In too many cases it is forgotten that the donor may often forfeit a meal time to answer a call

If, for some reason the transfusion does not take place, the donor naturally should be given a full explanation, and if necessary a written letter to take to his employers otherwise he may be unable to obtain leave in the future for a transfusion The *service should also be notified at once*, in order that the donor s name may be replaced on the list of those available

The technique to be adopted at the transfusion itself may well be left to the surgeon in charge but in this connexion it must be stressed that cutting down is quite inadmissible that a local anaesthetic should be offered that no direct transfusion should take place without first obtaining the donor s permission, and that the recumbent position should always be used when drawing the blood The arguments against cutting down have been discussed elsewhere and the reasons for the offer of an anaesthetic are sufficiently apparent The recommendation that direct transfusion should not be given arises from the fact that the feelings of the donors who are sometimes of a very sensitive nature, must not be distressed by contact with their patient or with any other In addition the blood must not be drawn in the presence of the donor or in an occupied ward and discussions of technique should not take place in his presence With

reference to the principle that the recumbent position should be used in drawing blood, it may be pointed out that, during the last four years, all cases of the fainting of a donor after transfusion have followed the withdrawal of blood whilst the donor was seated in a chair. The donor should also be recommended to remain prone for at least ten minutes after withdrawal, although many of the veteran members of a service can dispense with this safeguard.

When the withdrawal of blood has actually taken place, considerate treatment of the donor should naturally continue A nurse should stay with the donor and take care that his arm is properly dressed and that any refreshment he wants is supplied. Finally, she should see him out of the hospital with a few words of thanks. It is not unusual for the whole of those present when the blood is withdrawn, afterwards to forget the existence of the donor in their interest in the transfusion of his blood into the patient. The donor is sometimes left without attention, and without his arm being dressed, for half an hour or more, and occasions can be quoted when the donor has been left to find his way out of a large institution in the night hours with no one to direct him

Apart from the treatment in the hospital, experience has shown that the question of the *recognition of the services* of the donor after a transfusion are of great importance Generally speaking, a donor will not serve again until he has had a report of the transfusion, naturally reasoning that, if the hospital has not sufficient courtesy to supply one, the organization should not be prepared to provide more donors. It is for this reason, therefore, that service should press the hospitals to forward immediately a complete answer to its questionnaire relating to the indications and result of a transfusion.

In recognizing the services of the donor, it is the rule of the London Blood Transfusion Service to *deal at once* with expenses and complaints, and the donor is urged to supply a full report by telephone or in writing within twenty-four hours of the transfusion. The donor's expenses are refunded immediately they are notified. As a general rule, expenses are moderate, averaging under one shilling per case, and rarely amounting to over five shillings except in the case of night calls

Circularization of Donors

The problem of keeping up a keen interest in the organization is met in London to some extent by the issue of a small Quarterly Circular containing statistics, reports of interesting cases, popularly written notes on technique, and provincial and foreign news items. This is circulated free (to all London and provincial members, and is very popular) and is valuable in providing accurate information to counterbalance press misstatements.

Resignations.

The adoption of the principles outlined above will probably constitute all that a service can do in the sphere of retaining the donor. The great factor causing resignations with which it is particularly difficult to deal is the power of the press, and this can be modified in the right direction only by a gradual popularization of the idea of transfusion as a social service to which no *danger or expense* is attached. Since the press itself is unwittingly the most detrimental agent against the enlightenment of the public, a vicious circle results out of which the way is not yet clear. Some quotations may indicate the difficulty of the problem.

> Firemen are now being asked to give their blood in transfusions at Evanston, Illinois, because the local police commissioner complains that his constables are beginning to look anaemic through giving too much.

From nearer home comes a surprising account of a transfusion which is surely calculated to deter the most heroic.

> After a hasty rush home for a personal record card—both arms were then thoroughly cleansed with chemicals whilst a doctor estimated my fitness for the task ahead. My arms were then swathed in warm blanket material and I was directed to lie on a trolley which was pushed into the theatre. After the withdrawal of the blood I was again placed upon a trolley and almost completely covered in blankets which had been heating in readiness. Having been wheeled into a side ward I received a welcome stimulant and an injunction to lie quietly for a time. Roughly two hours after the transfusion the doctor said I should soon be all right to get away. The bandage was now removed and two stitches inserted in the wound, which had by this time ceased to bleed. I was now allowed to get up from the trolley and on going away received instructions to report back the following week to have the stitches removed.

Again, such misstatements as 'only one of the four groups can

SUMMARY

Advantages and disadvantages of the two systems

A voluntary system is to be preferred to a professional one its chief advantage being the low cost of maintenance and the *better type of donor enrolled*

Principles involved in the formation and management of a voluntary service

Obtaining the donor Recruiting of reliable donors by lectures pamphlets advertisement and broadcasting with reference to the special merits and limitations of each form of propaganda

The value of personal recommendations by donors

Transfusion not to be portrayed as an act of heroic self sacrifice but as a social service beneficial to the donor and involving no *financial* outlay and no personal *inconvenience* other than loss of time

Retaining the donor Difficulties encountered suggest the following methods of procedure

A The establishment of a central office to direct the organization *independently* of hospitals or other institutions and to be responsible for—

1 Calling up the donors *in rotation* This is the most *important subsidiary principle* and *mismanagement* of this aspect is the commonest cause of collapse of a transfusion service

2 Seeing that the universal donor is not called up disproportionately

3 Seeing that a new donor receives an early call and an experienced surgeon

(Various methods of calling up the donor are suggested)

B The establishment of a representative committee to deal with the general interests of the donor by considering his suggestions and complaints

C The appointment of a medical officer to be responsible *for the selection of donors and the subsequent care of* their health

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give blood—the other three corrode'; 'greatly weakened condition of the donor'; 'not more than one person in fifty has the right physique to give blood'—and, referring to a professional footballer, 'he was able to play, to the amazement of his doctor, eight days later', are to be read almost daily in the newspapers and must have a most unfortunate effect upon the minds of relatives and friends of prospective donors

The press would be doing a valuable public service if they could increase the confidence of the public in the matter, by allaying the unfounded prejudices which are so widely believed

CALLING UP OF DONORS

The most important subsidiary principle in the running of a Blood Transfusion system is that governing the calling up of donors. *The commonest cause of collapse of transfusion services* is mismanagement of this aspect of the work, and this usually takes the form of an unequal demand upon the services of the individual donors. This may come about in two ways There may be a disproportionate demand by hospitals for members of the so-called 'universal donor' group, or there may be a disproportionate calling up by the Service of the donors who are most readily accessible to it. In the former case a particular blood group is used excessively, and in the latter particular individuals. In either case one body of donors receives calls so frequently as to tire them of the service, whereas others who are only used occasionally lose interest and drift away In the case of the drain on donors of group O, there is the additional disadvantage that this group alone is available for answering emergency calls. The excessive demand for universal donors arises as a result of hospital authorities taking the line of least resistance, and omitting grouping on principle, or by failing to look ahead and group all possible candidates for transfusion on admission.

Abuse of the universal donor.

In 1929 the demands for group O donors from the London Blood Transfusion Service reached the disproportionate figure of 66 per cent., whereas only 25 per cent. of the calls were for group A—yet normally the two groups are present in the

population and amongst the donors of service in almost equal numbers (about 45 per cent) Even allowing for a certain number of gravely urgent calls where there was no possibility of grouping it was obvious that group O s were being called up unnecessarily with the result that a serious scarcity of group O s was experienced The matter was carefully considered It was felt that blood grouping was such a simple and expeditious operation that the lack or absence of a pathologist or the non possession of serum should not be accepted as adequate reasons for not grouping It was further felt that any patient for whom there was the slightest possibility of a transfusion being required should be grouped automatically upon entering hospital and that it was no excuse to say several days after admission that there had been no time to group

It was therefore resolved to instruct the office staff *to refuse all calls for universal donors where the patient had not been grouped* unless entirely satisfactory reasons for the non grouping were received and further to urge that all calls for bona fide group O cases be postponed until after business hours when possible

A great deal of unpleasantness was occasioned by the carrying out of these instructions but a markedly reduced demand for universal donors has been the outcome so that in 1930 0 per cent of the calls were for O s and 30 per cent for A s and this in spite of an increase of more than 2 000 calls per annum in the interval (Fig 15)

Donors in rotation.

The second common factor of mismanagement is the failure to call up donors in rotation It has been found that the circumstances in which this is most likely to occur are when the calling up of individual donors rests in the hands of the hospital authorities or individual surgeons This task soon becomes delegated to a junior official such as a telephone girl or hall porter whose only object is to obtain a donor with a minimum *of trouble Inevitably this results in the calling up of the person* most easily reached by telephone and that donor becomes overworked while those not so readily accessible rarely if ever receive calls In this connexion it may be noted that in London for example opportunities are usually given of summoning donors

from some little distance, since less than one-third of the total number of calls are of real urgency, while some give one to three days' notice. There is, therefore, no adequate excuse for the overworking of particular donors, especially as the principle of rotation is so vital to the success of a service.

The solution of the difficulty lies in the formation of a *separate organization with its own central office, to carry out, independently of the hospital staff*, medical or administrative, the work of the organization. This central bureau, in addition to enforcing rotation among the donors, will also be the most effective safeguard against a disproportionate demand for the service of members of the universal donor group, provided it is in the hands of an individual of sufficient personality to deal with summary and unreasonable demands from hospitals

The organization in adopting such a course of action must have, for obvious reasons, the unqualified support of the medical practitioners in the district served

Another argument which may be raised in support of a separate organization is that when a hospital runs its own Service—without the intervention of a local committee—it may find itself in competition with other hospitals in the same area, a very undesirable state of affairs, which is likely to lead to the introduction of payment as an inducement to serve

A central office could be conveniently established in the house of a private individual whose telephone is never left (as is the case with the London Blood Transfusion Service), or in a Y.M.C A. or Toc H Hostel or a nursing home or ambulance station: it could take over those methods of procedure, the success of which in practice has already been demonstrated by the voluntary services in London, Liverpool, Birmingham, Newcastle, Bristol, and other parts of the country.

Calling up a Donor: the procedure

The general principles to be followed in calling up donors have been stressed, but something must also be said about the actual methods and procedure to be adopted by a Central Office in calling up individual donors. The method of the London Blood Transfusion Service may be taken as a guide.

Immediate procedure.

When the Service receives a call it first inquires the name of the hospital, the ward, the name and group of the patient and the surgeon who will carry out the transfusion The records are then consulted and a donor is supplied in strict rotation and of the right blood group From the main register of available donors, a district register (particularly useful after business hours since it gives the number of donors available in the vicinity of a given hospital) and a card index, the particulars of all possible donors can be obtained at a glance Besides blood group, times available and accessibility details such as special objections to and preference for particular hospitals, dates and hospitals of previous transfusions and such comments as 'Novice, not yet used , Particularly available for night calls', appear at once

Methods available

9 a m to 6 p m.

Having selected a suitable donor steps are now taken to get in touch with him as quickly as possible Various methods are practised by the London Blood Transfusion Service During business hours that is to say from 9 a m to 6 p m , most calls are served by officials and employees of professional and business houses who are obtained by *telephone*

6 p m to 8 p m

From 6 p m to 8 p m express messages, that is to say telegrams telephoned to the nearest post office, are utilized, the donor being asked to telephone at once for full instructions

After 8 p m

After 8 p m there are various methods of getting in touch with the donor

(*a*) By telephoning the very few donors who are available by private telephone

(*b*) By telephoning friends or neighbours who have volunteered to inform the donor

(*c*) By telephoning members of rotary clubs a considerable number of whom in London have given their promise to call up donors within their immediate vicinity

(*d*) By telephoning the nearest police station and asking them to send a constable Although this request is never refused it is not a very reliable method since the officer may be called upon either going or returning to perform ordinary constabulary duties

(*e*) By telephoning all night garages and hiring a private car to call at address after address until a donor is found at home This is effective in the long run but very expensive

(*f*) By telephoning a taxi rank This is the weakest method of all, as many drivers will go to the house indicated and simply state they have brought the taxi ordered which may puzzle even the most intelligent donor

Post-transfusional procedure.

When a donor has been used his name is withdrawn from the list of available members only when he has intimated his willingness to serve at a further transfusion is it replaced

Insurance

In the general aspect of safeguarding the donor it should be noted that the question of insurance has arisen often and has always been rejected by the London Blood Transfusion Service The idea of insuring the donor is unpopular largely on account of the cost There is no basis available to compute probable claims and consequently Insurance Companies would safeguard themselves by a high premium One Insurance Company recently would not accept a policy on the life of a donor, thus showing the misapprehension that exists even in what should be well informed circles A tentative inquiry for terms recently elicited a quotation of an annual premium which far exceeded the total amount paid in compensation by the service during the ten years of its existence

In addition to the cost there are other reasons against insurance of donors There would possibly be a lessening of the responsibility of surgeons carrying out transfusions if they knew that the donor was insured against ill-effects, and on the other hand the donor might be tempted, if insured, to malinger for a few days Perhaps the greatest difficulties involved in the

principle of insurance lie in determining the liability for disablement and in the probability of claims being tendered which do not arise from transfusion *per se* In connexion with the first difficulty it may be noted that most cases have been of septic arms or burns or damage to clothing due to the use of iodine Unless these injuries were expressly covered—necessitating a higher premium—the Company would claim a refund from the hospital the latter would probably repudiate the claim and the Company on this showing would refuse to pay the donor

In connexion with claims which do not arise from transfusions themselves the service occasionally gets cases of sepsis or abscesses occurring long after transfusion but near the site of the puncture These are coincidences and no Insurance Company would pay claims for them On the other hand if the service were to disclaim liability the effect would be harmful to the organization since it is usually impossible to persuade such an individual that his trouble would have occurred if no blood transfusion had been given

The result of the drawbacks attending the project of insurance of a donor is that in this country the British Red Cross Society has decided to accept the entire responsibility for all claims occurring in the London and affiliated provincial services

Finance (see also cost pp 333, 334 336 337)

Finance is as a rule the aspect which causes the promoter of a new service the greatest anxiety Experience has proved however that it need not be a source of worry provided the organization is run along the lines already indicated If the right type of donor is obtained from the beginning a self supporting organization is built up if the wrong type is obtained—a type that is unreliable or withdrawn after one or two services—money is wasted on needless propaganda and office expenses Extravagant recruiting by expensive travel hiring of large halls advertising and broadcasting have all been shown to be unnecessary and usually less effective in obtaining either quantity or quality in new recruits Expenses however, naturally do occur, though in the London area for 1938 they amounted to only 7*s* 6*d* a case (there were 6 628 transfusions)

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      (Various methods of calling up the donor are suggested.)

B. The establishment of a representative committee to deal with the general interests of the donor, by considering his suggestions and complaints.

C. The appointment of a medical officer to be responsible for the selection of donors and the subsequent care of their health.

D. A limited frequency of service.

E. A rule forbidding cutting down on the veins.

F. The care of the personal treatment of the donor in every stage of the transfusion.

G. The recognition of services, particularly in the form of a report on the result of the transfusion.

Finance. The cost of running a transfusion service is estimated.

The problem of insurance is discussed.

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APPARATUS AND ACCESSORIES

Information concerning all apparatus mentioned in this book can be obtained from the Genito Urinary Manufacturing Co Ltd Devonshire Street London, unless otherwise stated in the text

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